OL Organic Letters
pubs.acs.org/OrgLett
Letter

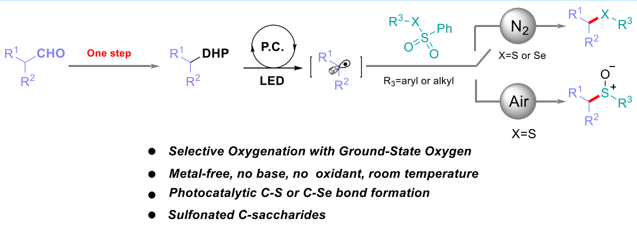
Visible-Light-Promoted Cross-Coupling Reactions of 4-Alkyl-1,4-dihydropyridines with Thiosulfonate or Selenium Sulfonate: A Unified Approach to Sulfides, Selenides, and Sulfoxides

Jian Li, Xin-Er Yang, Shan-Le Wang, Long-Long Zhang, Xiao-Zhou Zhou, Shun-Yi Wang,*
and Shun-Jun Ji*

Cite This: https://dx.doi.org/10.1021/acs.orglett.0c01776 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: In this paper, a visible-light-promoted cross-coupling of 4-alkyl-1,4-dihydropyridines with thio-/selenium sulfonates under transition-metal-free conditions is described. This strategy features easily available substrates, mild reaction conditions, high yields, and high chemoselectivity. A novel synthetic route for the construction of a sulfide or selenide C_{sp3}−S or C_{sp3}−Se bond under transition-metal-free conditions without an additive oxidant or base is developed. This method is well extended to the synthesis of a class of thiolated or selenylated glycosides that has not been explored before. Sulfoxides were also successfully chemoselectively observed via a facile variation of the atmosphere under photocatalyzed conditions.



- *Selective Oxygenation with Ground-State Oxygen*
- *Metal-free, no base, no oxidant, room temperature*
- *Photocatalytic C-S or C-Se bond formation*
- *Sulfonated C-saccharides*

Organosulfur compounds are widely used in chemical biology, medicinal chemistry, and pharmaceuticals. The development of new approaches for the construction of a C−S bond has attracted considerable attention.[1] The traditional method for the construction of C−S bond is the substitution reaction of organic halides and RSH (or RSSR).[2] However, these reactions have several drawbacks such as the unpleasant odor of sulfuration reagents, alkaline reaction conditions, high temperature, and expensive transition-metal catalysts. Developing efficient and mild methodologies for the construction of a C−S bond continues to be highly desirable. As a clean, efficient, and accessible strategy, photoredox catalysis has been recognized as a useful tool for the direct coupling of two electrophiles under mild conditions during the past decade.[3] Recently, the Fu and Miyake groups achieved the representative visible-light photoredox construction of C_{sp2}−S bonds (Figure 1, a).[4] While the visible-light mediated photoredox reactions to construct C_{sp2}−S bonds have been well developed, the construction of C_{sp3}−S bonds in this field are less reported. Wang, Xu, and Fu's groups successively reported the C_{sp3}−S construction reaction under visible-light conditions. However, these reactions often require equivalent amounts of base or oxidant with limited substrates (Figure 1, b).[5] Therefore, it is still very challenging to develop novel strategies to construct C_{sp3}−S bonds under visible-light conditions.

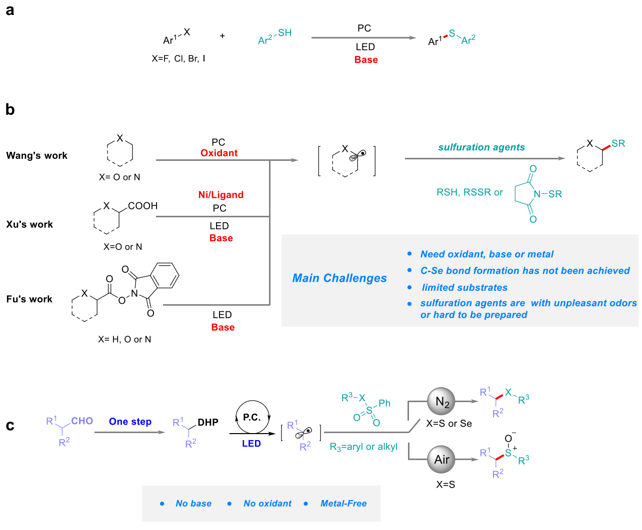


Figure 1. Visible-light photoredox construction of C−S bonds.

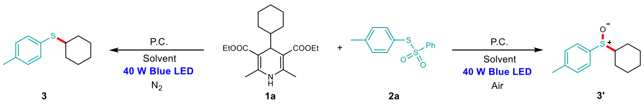
4-Alkyl-1,4-dihydropyridines (DHPs) can be readily prepared from aldehydes in one step with high functionalization levels. Since the pioneering work of Nishibayashi,[6] C−C bond cleavage of DHPs has emerged as an effective strategy to construct C_{sp3}−C_{sp2},[7] C_{sp3}−C_{sp}[8] C_{sp3}−N,[9] and C_{sp3}−X (X = Cl, Br, I)[10] bonds. In addition, Melchiorre's group recently reported a visible-light-mediated strategy that successfully

Received: May 26, 2020

couples symmetrical anhydrides and DHPs to afford enantioenriched α-substituted ketones under mild conditions.[11] To the best of our knowledge, in such an active field, the use of DHPs to construct C_{sp3}−S or C_{sp3}−Se bonds has not been achieved. Very recently, our group has achieved a nickel-catalyzed reductive thiolation and selenylation of unactivated alkyl bromides[12] and a nickel-catalyzed defluorinative reductive cross-coupling of *gem*-difluoroalkenes with thio-/selenosulfonates.[13] As a novel sulfuration reagent, benzenesulfonothioate[14] has some advantages compared to other sulfuration agents (thiols, disulfides, sulfenyl halides, sulfonium salts, *N*-thioimide quinone mono *O*,*S*-acetals, *p*-toluenesulfonyl hydrazide *S*-acetals, arylsulfonyl chlorides, sulfinic acids, and *p*-tolylsulfinate)[15] such as being stable to air, without unpleasant odors, and easy to prepare. Based on our previous investigation of the thio-/selenosulfonates, we wonder whether thio-/selenosulfonates might trap the radicals generated by DHPs. If so, construction of C_{sp3}−S bonds would be accessible under photocatalyzed conditions. Herein, we reported a visible-light-promoted cross-coupling of 4-alkyl-1,4-dihydropyridines with thio-/selenosulfonates (Figure 1, c). This protocol provided a novel synthetic route for the construction of C_{sp3}−S bonds or C_{sp3}−Se bonds under metal-free conditions. No metal, alkali, or oxidant involvement is required compared to previous reports.

Initially, we studied the model reaction of cyclohexyl-DHP (**1a**) with *S*-(*p*-tolyl) benzenesulfonothioate (**2a**) in MeCN catalyzed by *fac*-Ir(ppy)$_3$ under irradiation of 40 W blue LED light. To our delight, it was found that the desired cyclohexyl(*p*-tolyl)sulfane **3** was obtained in 77% isolated yield (Table 1, entry 1). No desired product was detected in the absence of photocatalyst or in the dark (Table 1, entries 2 and 3). These results indicate that both photocatalyst and visible-light irradiation are absolute requirements for this reaction. We further examined the effect of other photocatalysts ([Ir(dtbbpy)(ppy)$_2$][PF$_6$], EosinY and 4-CzIPN). 4-CzIPN ($6.01/g) is the best choice for this reaction (Table 1, entries 4−6). Next, we screened reaction solvents. When DMF was applied to the reaction, **3** was observed in 53% yield (Table 1, entry 7). It should be noted that the reaction of **1a** and **2a** in DCE gave **3** in 85% yield (Table 1, entry 8). After carefully studying the reaction concentration, it was found that 2 mL of DCE was the ideal amount for this reaction and the yield of **3** was increased to 99% (Table 1, entries 9 and 10). Notably, by only altering the atmosphere to air, 1-(cyclohexylsulfinyl)-4-methylbenzene **3′** was obtained in 95% isolated yield (Table 1, entry 11).

Table 1. Screening of Reaction Conditions[a]

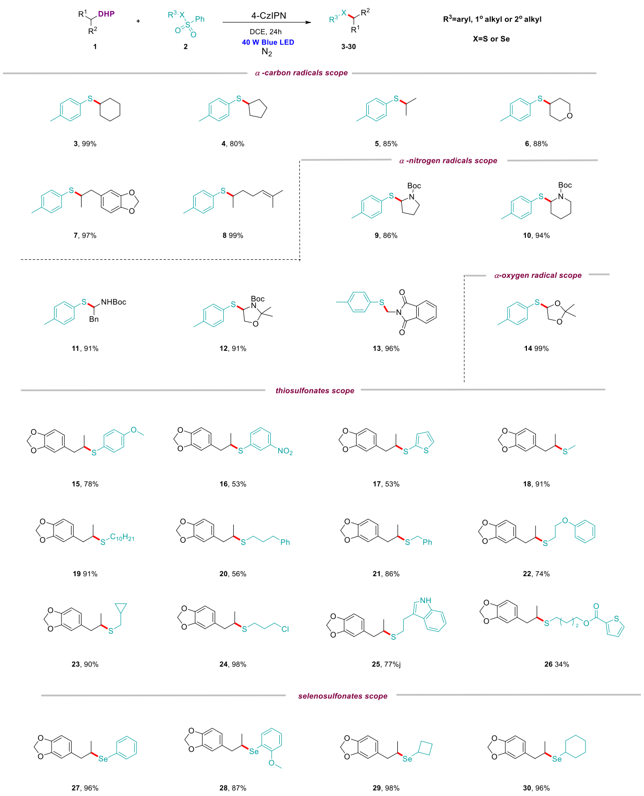


			yield[b] (%)	
entry	P.C.	solvent	3	3′
1	*fac*-Ir(ppy)$_3$	MeCN (1)	77	0
2	*fac*-Ir(ppy)$_3$	MeCN (1)	0	0
3[c]	*fac*-Ir(ppy)$_3$	MeCN (1)	0	0
4	[Ir(dtbbpy)(ppy)$_2$][PF$_6$]	MeCN (1)	64	0
5	EosinY	MeCN (1)	76	0
6	4-CzIPN	MeCN (1)	81	0
7	4-CzIPN	DMF(1)	53	0
8	4-CzIPN	DCE (1)	85	0
9	4-CzIPN	DCE (1.5)	91	0
10	4-CzIPN	DCE (2)	99	0
11[d]	4-CzIPN	DCE (2)	0	95

[a]Reaction conditions: diethyl 4-cyclohexyl-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (**1a**, 0.30 mmol), *S*-(*p*-tolyl) benzenesulfonothioate (**2a**, 0.10 mmol), P.C. (3 mol %), in solvent at room temperature for 24 h under N$_2$, 40 W LED. [b]Yields were determined by GC. [c]In the dark. [d]Under air.

With the optimized conditions in hand, we evaluated the synthetic potential of this photomediated reaction (Table 1). First, we focused our attention on radical precursors (Scheme 1). Importantly, secondary alkyl radicals such as cyclohexyl radical, cyclopentyl radical, and isopropyl radical are tolerated well in this transformation (**3-5**). A pyran-derived DHP could likewise be used, and the resulting sulfide was isolated in 88% yield (**6**). Diethyl 4-(1-(benzo[d][1,3]dioxol-5-yl)propan-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate was also tolerated under this transformation (**7**). More interestingly, alkyl radicals bearing distal alkenes were compatible with such mild reaction conditions (**8**). α-Nitrogen radicals were also tested, and a series of *N*,*S*-acetal derivatives were furnished in excellent yields (**9**−**12**). Similar results were achieved for primary alkyl radical (**13**). α-Oxygen radicals could also be employed, which brought about the introduction of dioxolane motif (**14**).

Scheme 1. Substrate Scope of Various DHPs, Thiosulfonates, and Selenosulfonates[a,b]

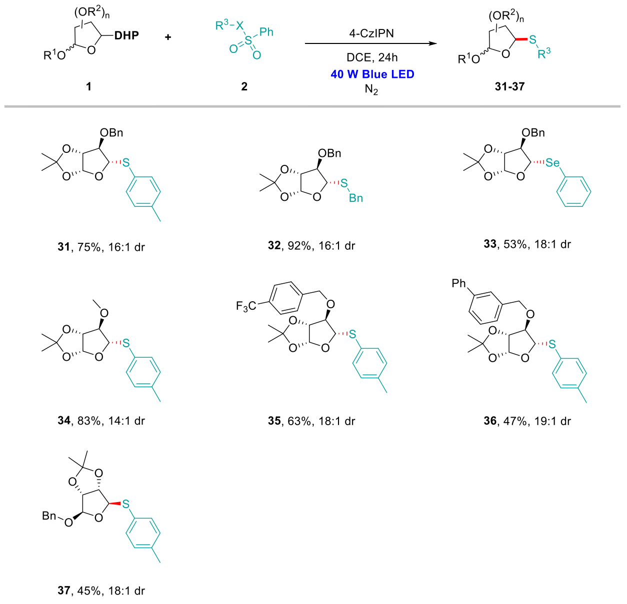


[a]Standard conditions: **1** (0.6 mmol), **2a** (0.2 mmol), 4-CzIPN (3 mol %), DCE (4 mL), 40 W LED, rt under N$_2$ for 24 h. [b]Isolated yields.

Next, we turned our attention to investigate whether other sulfonothioates can be employed as radical receptors using diethyl 4-(1-(benzo[*d*][1,3]dioxol-5-yl)propan-2-yl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate as a radical precursor (Scheme 1). For *S*-aryl benzenesulfonothioates, both electron-donating (OMe) and electron-withdrawing (NO_2) substituents were well tolerated in the meta and para positions so that products **15** and **16** could be isolated in 78% and 53% yields. When *S*-(Het) benzenesulfonothioate was used for the reaction, the desired product **17** could be obtained in 53% yield. Subsequently, a series of *S*-alkyl benzenesulfonothioates were investigated, and the corresponding alkyl–alkyl sulfides **18–23** could be obtained under standard conditions. It should be noted that the use of DHPs allowed a room temperature set of reaction conditions, in contrast with previous reports that generally require 60–100 °C.[12,13] It is worth mentioning that substituents bearing functionalized groups such as chlorine, indole, and thiophene could also be accommodated under the mild reaction conditions to afford the desired products **24–26** in moderate to good yields. Furthermore, the reactions of various *Se*- primary aryl benzenesulfonoselenoates could be successfully coupled with DHPs (adducts **27–28**). *Se*-Secondary alkyl benzenesulfonoselenoates were also investigated in the reactions with DHPs, and we could obtain the cyclobutyl and cyclohexyl (**29–30**) selenides in high yields.

Glycosyl thioacetals, as versatile glycosyl donors, have emerged as a class of important fragments because of their numerous synthetic applications.[16] Our protocol provides a simple strategy to directly prepare a range of glycosyl thioacetals from the corresponding DHPs under the mild conditions (Scheme 2). Upon treating furanose DHP with *S*-aryl benzenesulfonothioates under the standard reaction conditions, the nontraditional C-sulfenylated glycoside was isolated in 75% yield with excellent diastereoselectivity (**31**). *S*-Benzyl benzenesulfonothioates and *Se*-aryl benzenesulfonoselenoates are also amenable to this visible-light-promoted reaction (**32–33**). Less sterically constrainted furanose DHP performed equally well (**34**). The furanose DHPs with *ortho*- and *para*- groups on the aromatic rings were tested, and all of them reacted smoothly with *S*-aryl benzenesulfonothioates, yielding the desired products with high efficiency (**35** and **36**). Moreover, pyranose DHP could work well in the reactions with *S*-(*p*-tolyl) benzenesulfonothioate. We could obtain the corresponding product **37** in 45% yield with excellent 18:1 dr selectivity.

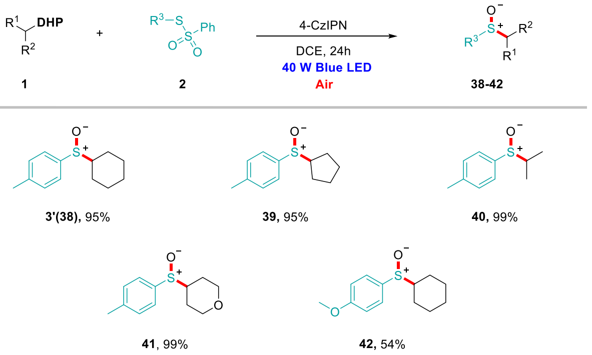
Scheme 2. Scope with Respect to Monosaccharides[a–c]



[a]Standard conditions: **1** (0.4 mmol), **2** (0.2 mmol), 4-CzIPN (3 mol %), DCE (4 mL), 40 W LED, rt under N_2 for 24 h. [b]Isolated yields [c]The dr selectivity was determined by ^1H NMR spectra.

On the other hand, by altering the atmosphere to air, a range of sulfoxides were efficiently obtained in high isolated yields (**38–40**) (Scheme 3). Moreover, electronic effects of substituents on both the DHPs and *S*-aryl benzenesulfonothioates did not affect the efficiency (**41** and **42**).

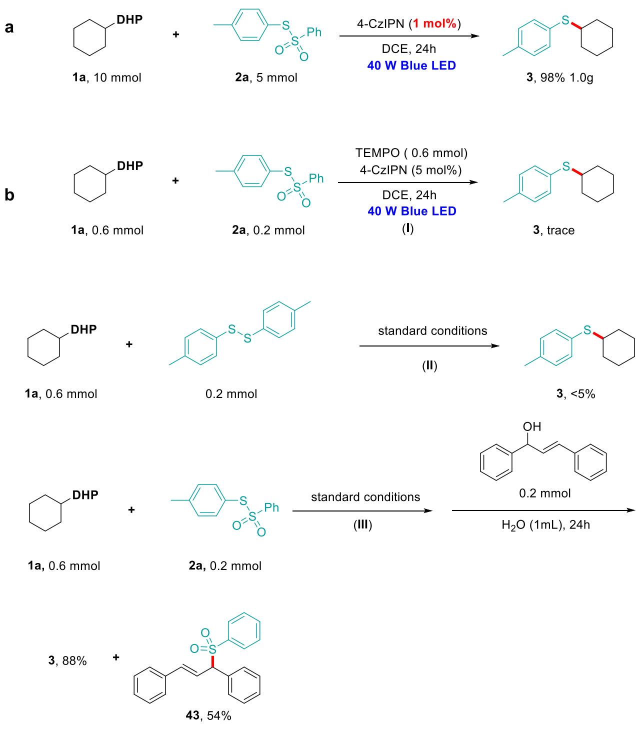
Scheme 3. Scope of Thiosulfonate[a,b]



[a]Standard conditions: **1c** (0.6 mmol), **2** (0.2 mmol), 4-CzIPN (3 mol %), DCE (4 mL), 40 W LED, rt under air for 24 h. [b]Isolated yields.

To evaluate the application of this visible-light-promoted cross-coupling reaction, the gram-scale reaction of **1a** (10 mmol) with **2a** (5 mmol) in the presence of only 1 mol % of 4-CzIPN was investigated (as shown in Scheme 4, a). The

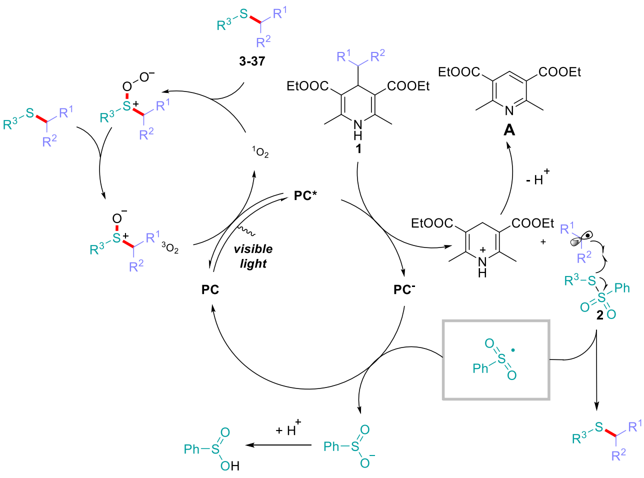
Scheme 4. Gram-Scale Reaction and Control Experiments



desired product **3** could also be obtained in 98% yield with lower catalyst loading. Subsequently, to preliminarily probe into the mechanism of the reaction, several control experiments were conducted (Scheme 4, b). When 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) as radical scavenger was added in this reaction system, a trace amount of adduct **3** was detected (Scheme 4, b, I), which revealed that a radical mechanism was involved in this transformation. The use of PhSSPh in place of **2a** resulted in only <5% yield of product **3**. This result indicates that PhSSPh was not the intermediate of this reaction (Scheme 4, b, II). Recenty, Loh's group reported a water-catalyzed reaction of sulfonic acid and allyl alcohol.[17] Encouraged by these interesting results, we added 1,3-diphenyl-2-enol and 1 mL of water to the reaction system directly without separation and then reacted the system for an additional 24 h. The formation of cyclohexyl(*p*-tolyl)sulfane (**3**) and (3-(phenylsulfonyl)prop-1-ene-1,3-diyl)dibenzene (**43**) was observed, indicating the formation of benzenesulfinic acid (Scheme 4, b, III). Addionally, through this novel strategy, we can improve the atomic economy of this strategy.

On the basis of the above results and literature reports,[7−10] a plausible reaction mechanism was proposed in Scheme 5. The photocatalyst 4-CzIPN assists the single electron transfer of the DHPs to generate an alkyl radical and pyridine **A**. Subsequently, alkyl radical reacts with sulfonothioates to afford a sulfone radical intermediate.[18] Then reductive SET of sulfone radical furnishes benzosulfinic acid anion. Subsequent protonation of benzosulfinic acid anion affords the benzosulfinic acid. On the other hand, $^1O_2$ can be generated from an energy-transfer process[19] between $^3O_2$ and 4-CzIPN*, which can oxidize the sulfide to the corresponding sulfoxide.

Scheme 5. Proposed Mechanism



In summary, we have developed a visible-light-promoted cross-coupling of 4-alkyl-1,4-dihydropyridines with thio-/selenium sulfonates. This strategy realized the construction of a C_{sp3}−S bond or C_{sp3}−Se bond under metal-free, oxidant-free, and base-free conditions, enabling access to thiolated or selenylated glycosides that has been underexplored until now. Moreover, sulfoxides were successfully tuned via a facile variation of the atmosphere under photocatalyzed conditions without any additional oxidant.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c01776.

Detailed experimental procedures (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

Shun-Yi Wang − *Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science and Collaborative Innovation Center of Suzhou Nano Science and Technology, Soochow University, Suzhou 215123, China*; orcid.org/0000-0002-8985-8753; Email: shunyi@suda.edu.cn

Shun-Jun Ji − *Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science and Collaborative Innovation Center of Suzhou Nano Science and Technology, Soochow University, Suzhou 215123, China*; orcid.org/0000-0002-4299-3528; Email: shunjun@suda.edu.cn

Authors

Jian Li − *Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science and Collaborative Innovation Center of Suzhou Nano Science and Technology, Soochow University, Suzhou 215123, China*

Xin-Er Yang − *Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science and Collaborative Innovation Center of Suzhou Nano Science and Technology, Soochow University, Suzhou 215123, China*

Shan-Le Wang − *Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science and Collaborative Innovation Center of Suzhou Nano Science and Technology, Soochow University, Suzhou 215123, China*

Long-Long Zhang − *Key Laboratory of Organic Synthesis of Jiangsu Province, College of Chemistry, Chemical Engineering and Materials Science and Collaborative Innovation Center of Suzhou Nano Science and Technology, Soochow University, Suzhou 215123, China*

Xiao-Zhou Zhou − *Suzhou High School of Jiangsu Province, Suzhou 215000, China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.0c01776

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We gratefully acknowledge the National Natural Science Foundation of China (21971174, 21772137, 21542015, and 21672157), PAPD, the project of scientific and technologic infrastructure of Suzhou (SZS201708), and the Major Basic Research Project of the Natural Science Foundation of the Jiangsu Higher Education Institutions (16KJA150002), Soochow University.

REFERENCES

(1) (a) Mitchell, S. C.; Nickson, R. M.; Waring, R. H. The Biological Activity of Selenium Sulfide. *Sulfur Rep.* **1993**, *13*, 279−289. (b) Liu, G.; Link, J. T.; Pei, Z.; Reilly, E. B.; Leitza, S.; Nguyen, B.; Marsh, K. C.; Okasinski, G. F.; Geldern, T. W.; Ormes, M.; Fowler, K.; Gallatin, M. Discovery of novel *p*-Arylthio Cinnamides as Antagonists of Leukocyte Function-Associated Antigen-1/Intracellular Adhesion Molecule-1 Interaction. 1. Identification of An Additional Binding Pocket Based on an Anilino Diaryl Sulfide Lead. *J. Med. Chem.* **2000**, *43*, 4025−4040. (c) McReynolds, M. D.; Dougherty, J. M.; Hanson, P. R. Synthesis of Phosphorus and Sulfur Heterocycles via Ring-Closing Olefin Metathesis. *Chem. Rev.* **2004**, *104*, 2239−2258. (d) Konaklieva, M. I.; Plotkin, B. J. Recent Pat. AntiInfect. Recent Patents on Anti-Infective Drug Discovery. *Recent Pat. Anti-Infect. Drug Discovery* **2006**, *1*, 177−180. (e) D'Angelo, N. D.; Kim, T.-S.; Andrews, K.; Booker, S. K.; Caenepeel, S.; Chen, K.; D'Amico, D.; Freeman, D.; Jiang, J.; Liu, L.; McCarter, J. D.; Miguel, T. S.; Mullady, E. L.; Schrag, M.; Subramanian, R.; Tang, J.; Wahl, R. C.; Wang, L.; Whittington, D. A.; Wu, T.; Xi, N.; Xu, Y.; Yakowec, P.; Yang, K.; Zalameda, L. P.; Zhang, N.; Hughes, P.; Norman, M. H. Discovery and Optimization of A Series of Benzothiazole Phosphoinositide 3-Kinase PI3K/Mammalian Target of Rapamycin mTOR Dual Inhibitors. *J. Med. Chem.* **2011**, *54*, 1789−1811. (f) Xu, X.-B.; Liu, J.; Zhang, J.-J.; Wang, Y.-W.; Peng, Y. Nickel-Mediated Inter- and Intramolecular C−S Coupling of Thiols and Thioacetates with Aryl Iodides at Room Temperature. *Org. Lett.* **2013**, *15*, 550−553.

(2) For selected examples, see: (a) Chauhan, P.; Mahajan, S.; Enders, D. Organocatalytic Carbon−Sulfur Bond-Forming Reactions. *Chem. Rev.* **2014**, *114*, 8807−8864. (b) Kim, J. K.; Bonicamp, J.; Caserio, M. C. Methoxymethyl Cations. 2. Reactions With Allylic Ethers and Sulfides in The Gas Phase. *J. Org. Chem.* **1981**, *46*, 4236−4242. (c) Krishnaveni, N. S.; Surendra, K.; Rao, K. R. Study of The Michael Addition of β-Cyclodextrin-Thiol Complexes to Conjugated Alkenes in Water. *Chem. Commun.* **2005**, 669−671. (d) Khatik, G. L.; Kumar, R.; Chakraborti, A. K. Catalyst-Free Conjugated Addition of Thiols to α,β-Unsaturated Carbonyl Compounds in Water. *Org. Lett.* **2006**, *8*, 2433−2436. (e) Firouzabadi, H.; Iranpoor, N.; Abbasi, M. A Facile Generation of C-S Bonds via One-Pot, Odourless and Efficient Thia-Michael Addition Reactions Using Alkyl, Aryl or Allyl Halides, Thiourea and Electron-Deficient Alkenes in Wet Polyethylene Glycol PEG 200 under Mild Reaction Conditions. *Tetrahedron* **2009**, *65*, 5293−5301.

(3) For selected reviews on visible-light photoredox catalysis, see: (a) 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*, 5322−5363. (b) Ravelli, D.; Dondi, D.; Fagnoni, M.; Albini, A. Photocatalysis. A Multi-Faceted Concept for Green Chemistry. *Chem. Soc. Rev.* **2009**, *38*, 1999−2011. (c) Narayanam, J. M. R.; Stephenson, C. R. J. Visible Light Photoredox Catalysis: Applications in Organic Synthesis. *Chem. Soc. Rev.* **2011**, *40*, 102−113. (d) Shi, L.; Xia, W. Photoredox Functionalization of C−H Bonds Adjacent to A Nitrogen Atom. *Chem. Soc. Rev.* **2012**, *41*, 7687−7697. (e) Yoon, T. P.; Ischay, M. A.; Du, J. Visible Light Photocatalysis as A Greener Approach to Photochemical Synthesis. *Nat. Chem.* **2010**, *2*, 527. (f) Tucker, J. W.; Stephenson, C. R. J. Shining Light on Photoredox Catalysis: Theory and Synthetic Applications. *J. Org. Chem.* **2012**, *77*, 1617−1622. (g) Kong, W.; An, H.; Song, Q. Visible-Light-Induced Thiotrifluoromethylation of Terminal Alkenes with Sodium Triflinate and Benzenesulfonothioates. *Chem. Commun.* **2017**, *53*, 8968−8971. (h) Wang, X.; Yang, M.; Xie, W.; Fan, X.; Wu, J. Photoredox-Catalyzed Hydrosulfonylation Reaction of Electron-Deficient Alkenes with Substituted Hantzsch Esters and Sulfur Dioxide. *Chem. Commun.* **2019**, *55*, 6010−6013.

(4) (a) Jiang, M.; Li, H.; Yang, H.; Fu, H. Room-Temperature Arylation of Thiols: Breakthrough with Aryl Chlorides. *Angew. Chem., Int. Ed.* **2017**, *56*, 874−879. (b) Liu, B.; Lim, C.-H.; Miyake, G. M. Visible-Light-Promoted C-S Cross-Coupling via Intermolecular Charge Transfer. *J. Am. Chem. Soc.* **2017**, *139*, 13616−13619.

(5) (a) Zhu, X.; Xie, X.; Li, P.; Guo, J.; Wang, L. Visible-Light-Induced Direct Thiolation at α-Csp^3-H of Ethers with Disulfides Using Acridine Red as Photocatalyst. *Org. Lett.* **2016**, *18*, 1546−1549. (b) Wei, L.; Wu, C.; Tung, C.-H.; Wang, W.; Xu, Z. Decarboxylative Sulfenylation of Amino Acids via Metallaphotoredox Catalysis. *Org. Chem. Front.* **2019**, *6*, 3224−3227. (c) Jin, Y.; Yang, H.; Fu, H. An *N*-Acetoxyphthalimide Motif as A Visible-Light Pro-Photosensitizer in Photoredox Decarboxylative Arylthiation. *Chem. Commun.* **2016**, *52*, 12909−12912.

(6) (a) Nakajima, K.; Nojima, S.; Sakata, K.; Nishibayashi, Y. Visible-Light-Mediated Aromatic Substitution Reactions of Cyanoarenes with 4-Alkyl-1,4-dihydropyridines through Double Carbon-Carbon Bond cleavage. *ChemCatChem* **2016**, *8*, 1028−1032. (b) Nakajima, K.; Nojima, S.; Nishibayashi, Y. Nickel-And Photoredox-Catalyzed Cross-Coupling Reactions of Aryl Halides with 4-Alkyl-1,4-dihydropyridines as Formal Nucleophilic Alkylation Reagents. *Angew. Chem., Int. Ed.* **2016**, *55*, 14106−14110. (c) Nakajima, K.; Guo, X.; Nishibayashi, Y. Cross-Coupling Reactions of Alkenyl Halides with 4-Benzyl-1,4-Dihydropyridines Associated with E to Z Isomerization Under Nickel and Photoredox Catalysis. *Chem. - Asian J.* **2018**, *13*, 3653−3657.

(7) (a) Chen, W.; Liu, Z.; Tian, J.; Li, M.; Ma, J.; Cheng, X.; Li, G. Building Congested Ketone: Substituted Hantzsch Ester and Nitrile as Alkylation Reagents in Photoredox Catalysis. *J. Am. Chem. Soc.* **2016**, *138*, 12312−12315. (b) Gutierrez-Bonet, A.; Tellis, J. C.; Matsui, J. K.; Vara, B. A.; Molander, G. A. 1,4-Dihydropyridines as alkyl radical Precursors: Introducing The Aldehyde Feedstock to Nickel/Photoredox Dual Catalysis. *ACS Catal.* **2016**, *6*, 8004−8008. (c) Goti, G.; Bieszczad, B.; Vega-Peñaloza, A.; Melchiorre, P. Stereocontrolled Synthesis of 1,4-Dicarbonyl compounds by Photochemical Organocatalytic Acyl Radical Addition to Enals. *Angew. Chem., Int. Ed.* **2019**, *58*, 1213−1217. (d) Song, Z.-Y.; Zhang, C.-L.; Ye, S. Visible Light Promoted Coupling of Alkynyl Bromides and Hantzsch Esters for The Synthesis of Internal Alkynes. *Org. Biomol. Chem.* **2019**, *17*, 181−185. (e) Wang, X.; Li, H.; Qiu, G.; Wu, J. Substituted Hantzsch Esters as Radical Reservoirs with The Insertion of Sulfur Dioxide under Photoredox Catalysis. *Chem. Commun.* **2019**, *55*, 2062−2065. (f) Phelan, J. P.; Lang, S. B.; Sim, J.; Berritt, S.; Peat, A. J.; Billings, K.; Fan, L.; Molander, G. A. Open-Air Alkylation Reactions in Photoredox-Catalyzed DNA-Encoded Library Synthesis. *J. Am. Chem. Soc.* **2019**, *141*, 3723−3732. (g) Nakajima, K.; Nojima, S.; Sakata, K.; Nishibayashi, Y. Visible-Light-Mediated Aromatic Substitution Reactions of Cyanoarenes with 4-Alkyl-1,4-dihydropyridines through Double Carbon−Carbon Bond Cleavage. *ChemCatChem* **2016**, *8*, 1028−1032.

(8) (a) Liu, X.; Liu, R.; Dai, J.; Cheng, X.; Li, G. *Org. Lett.* **2018**, *20*, 6906. (b) Song, Z.-Y.; Zhang, C.-L.; Ye, S. Visible Light Promoted Coupling of Alkynyl Bromides and Hantzsch Esters for The Synthesis of Internal Alkynes. *Org. Biomol. Chem.* **2019**, *17*, 181−185.

(9) Nakajima, K.; Zhang, Y.; Nishibayashi, Y. Alkylation Reactions of Azodicarboxylate Esters with 4-Alkyl-1,4-dihydropyridines under Catalyst-Free Conditions. *Org. Lett.* **2019**, *21*, 4642−4645.

(10) Liang, S.; Kumon, T.; Angnes, R. A.; Sanchez, M.; Xu, B.; Hammond, G. B. Synthesis of Alkyl Halides from Sldehydes via Deformylative Halogenation. *Org. Lett.* **2019**, *21*, 3848−3854.

(11) Gandolfo, E.; Tang, X.; Roy, S. R.; Melchiorre, P. Photochemical Asymmetric Nickel-Catalyzed Acyl Cross-Coupling. *Angew. Chem., Int. Ed.* **2019**, *58*, 16854−16858.

(12) Fang, Y.; Rogge, T.; Ackermann, L.; Wang, S.-Y.; Ji, S.-J. Nickel-Catalyzed Reductive Thiolation and Selenylation of Unactivated Alkyl Bromides. *Nat. Commun.* **2018**, *9*, 2240.

(13) Li, J.; Rao, W.; Wang, S.-Y.; Ji, S.-J. Nickel-Catalyzed Defluorinative Reductive Cross-Coupling Reaction of *gem*-Difluoroalkenes with Thiosulfonate or Selenium Sulfonate. *J. Org. Chem.* **2019**, *84*, 11542−11552.

(14) For selected examples, see: (a) Mampuys, P.; Zhu, Y.; Vlaar, T.; Ruijter, E.; Orru, R. V. A.; Maes, B. U. W. Sustainable Three-Component Synthesis of Isothioureas from Isocyanides, Thiosulfonates, and Amines. *Angew. Chem., Int. Ed.* **2014**, *53*, 12849−12854.

(b) Li, J.; Zhu, D.; Lv, L.; Li, C.-J. Radical Difluoromethylthiolation of Aromatics Enabled by Visible Light. *Chem. Sci.* **2018**, *9*, 5781−5786. (c) Zhao, X.; Zheng, X.; Tian, M.; Tong, Y.; Yang, B.; Wei, X.; Qiu, D.; Lu, K. Visible-Light Photocatalytic Trifluoromethylthiolation of Aryldiazonium Salts: Conversion of Amino Group into Trifluoromethylthiol Group. *Org. Chem. Front.* **2018**, *5*, 2636−2640. (d) Ghiazza, C.; Debrauwer, V.; Billard, T.; Tlili, A. A. Exploring The Reactivity of Trifluoromethyl Tolueneselenosulfonate with Alkynes Under Copper Catalysis. *Chem. - Eur. J.* **2018**, *24*, 97−100. (e) Ghiazza, C.; Debrauwer, V.; Monnereau, C.; Khrouz, L.; Médebielle, M.; Billard, T.; Tlili, A. Visible-Light-Mediated Metal-Free Synthesis of Trifluoromethylselenolated Arenes. *Angew. Chem., Int. Ed.* **2018**, *57*, 11781−11785.

(15) For selected examples on sulfuration agents, see: (a) Ge, W.; Wei, Y. Copper(I) Iodide Catalyzed 3-Sulfenylation of Indoles with Unsymmetric Benzothiazolyl-Containing Disulfides at Room Temperature. *Synthesis* **2012**, *44*, 934−940. (b) Ge, W.; Wei, Y. Iodine-Catalyzed Oxidative System for 3-Sulfenylation of Indoles with Disulfides Using DMSO as Oxidant Under Ambient Conditions in Dimethyl Carbonate. *Green Chem.* **2012**, *14*, 2066−2070. (c) Jain, S.; Shukla, K.; Mukhopadhyay, A.; Suryawanshi, S. N.; Bhakuni, D. S. The Reaction of Acyloxysulfonium Salt with Cyclic Enol Ethers: Novel Synthesis of Vinyl Sulfides. *Synth. Commun.* **1990**, *20*, 1315−1320.

(16) (a) Codee, J. D. C.; Litjens, R. E. J. N.; van den Bos, L. J.; Overkleeft, H. S.; van der Marel, G. A. Thioglycosides in Sequential Glycosylation Strategies. *Chem. Soc. Rev.* **2005**, *34*, 769−782. (b) Goswami, M.; Ellern, A.; Pohl, N. L. Bismuth(V)-Mediated Thioglycoside Activation. *Angew. Chem., Int. Ed.* **2013**, *52*, 8441−8445. (c) Goswami, M.; Ashley, D. C.; Baik, M. H.; Pohl, N. L. Mechanistic Studies of BismuthV-Mediated Thioglycoside Activation Reveal Differential Reactivity of Anomers. *J. Org. Chem.* **2016**, *81*, 5949−5962. (d) Vibhute, A. M.; Dhaka, A.; Athiyarath, V.; Sureshan, K. M. A Versatile Glycosylation Strategy via AuIII Catalyzed Activation of Thioglycoside Donors. *Chem. Sci.* **2016**, *7*, 4259−4263. (e) Lacey, K. D.; Quarels, R. D.; Du, S.; Fulton, A.; Reid, N. J.; Firesheets, A.; Ragains, J. R. Acid-Catalyzed O-Glycosylation with Stable Thioglycoside Donors. *Org. Lett.* **2018**, *20*, 5181−5185. (f) Saliba, R. C.; Wooke, Z. J.; Nieves, G. A.; Chu, A. A.; Bennett, C. S.; Pohl, N. L. B. Challenges in The Conversion of Manual Processes to Machine-Assisted Syntheses: Activation of Thioglycoside Donors with Aryltrifluoroethyliodonium Triflimide. *Org. Lett.* **2018**, *20*, 800−903. (g) Zhu, F.; Miller, E.; Zhang, S.-Q.; Yi, D.; O'Neill, S.; Hong, X.; Walczak, M. A. Stereoretentive Csp^3−S Cross-Coupling. *J. Am. Chem. Soc.* **2018**, *140*, 18140−18150.

(17) Xie, P.; Wang, J.; Liu, Y.; Fan, J.; Wo, X.; Fu, W.; Sun, Z.; Loh, T.-P. Water-Promoted C-S Bond Formation Reactions. *Nat. Commun.* **2018**, *9*, 1321.

(18) Carta, P.; Puljic, N.; Robert, C.; Dhimane, A.-L.; Ollivier, C.; L. Fensterbank, C.; Lacôte, E.; Malacria, M. CenterIntramolecular Homolytic Substitution at The Sulfur Atom: an Alternative Way to Generate Phosphorus- and Sulfur-ed Radicals. *Tetrahedron* **2008**, *64*, 11865−11875.

(19) (a) Nevesely, T.;´Svobodova, E.; Chudoba, J.; Sikorski, M.; Cibulka, R. Efficient Metal-Free Aerobic Photooxidation of Sulfides to Sulfoxides Mediated by A Vitamin B$_2$ Derivative and Visible Light. *Adv. Synth. Catal.* **2016**, *358*, 1654−1663. (b) Bonesi, S. M.; Manet, I.; Freccero, M.; Fagnoni, M.; Albini, A. Photosensitized Oxidation of Sulfides: Discriminating Between The Singlet-Oxygen Mechanism and Electron Transfer Involving Superoxide Anion or Molecular Oxygen. *Chem. - Eur. J.* **2006**, *12*, 4844−4857. (c) Clennan, E. L. *Acc. Chem. Res.* **2001**, *34*, 875. (d) Li, Y.; Wang, M.; Jiang, X. Controllable Sulfoxidation and Sulfenylation with Organic Thiosulfate Salts via Dual Electron- and Energy-Transfer Photocatalysis. *ACS Catal.* **2017**, *7*, 7587−7592.