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Oxime Ether Synthesis through O−H Functionalization of Oximes with Diazo Esters under Blue LED Irradiation

Qian Li, Bao-Gui Cai, Lei Li, and Jun Xuan*

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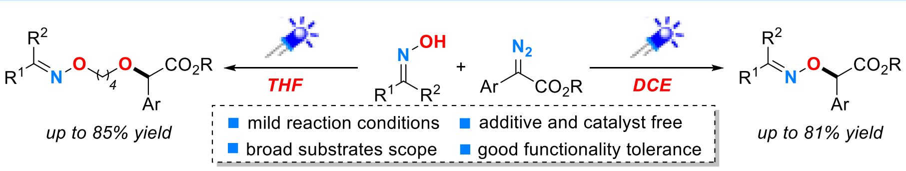
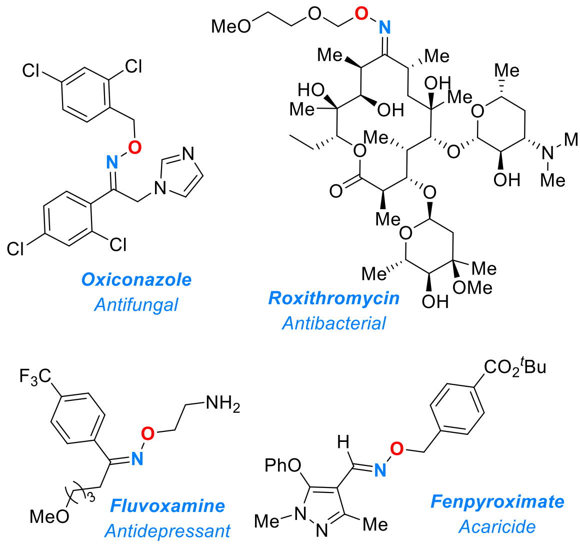


ABSTRACT: A green and sustainable oxime ether formation method via the visible-light-promoted O−H functionalization of oximes with diazo esters is described. The reaction occurs under very mild conditions (catalyst- and additive-free) with a high yield and a high functional group tolerance. When the reaction was performed with a cyclic ether as the solvent (e.g., THF, 1,4-dioxane, tetrahydropyran, ect.), an interesting photochemical three-component reaction product was obtained in good yields.

Oxime ether is one of the most important organic compounds.[1] Molecules containing oxime ether moieties can not only be frequently found in various medicines, showing excellent drug activity,[2] but can also be applied as the synthetic building blocks in synthetic organic chemistry.[3] Some compounds, such as the selected examples are shown in Scheme 1, are used to treat infections caused by bacteria, including the antifungal drug oxiconazole and the antibacterial drug roxithromycin, which contain the oxime ether scaffold.[2a−c] Fluvoxamine is used to treat obsessive-compulsive disorder and exhibits antidepressant activity.[2d,e] In addition, Fenpyroximate is a broad spectrum acaricide.[2f,g] Driven by their rich biological activities, the development of efficient and practical methods for the synthesis oxime ether is of widespread interest in synthetic organic chemistry.

Scheme 1. Bioactive Molecule Structures Containing Oxime Ether Motifs



In the past several years, a great deal of effort has been reported for oxime ether synthesis in both industry and academia. Traditionally, oxime ethers can be accessed through the condensation of carbonyl compounds with hydroxylamines, which usually requires additional catalysts or additives to accelerate the dehydration process (Scheme 2a).[4] The cross-coupling of oximes with arylboronic acids or organic halides is another elegant route to form oxime ether (Scheme 2b).[5,6] However, those methods generally require the use of transition-metal catalysts in high reaction temperatures. In addition, the allylic substitution of oximes in the presence of transition-metal catalysts to obtain oxime ether has also attracted much attention (Scheme 2c).[7] Compared with those well-developed methods, the continuous development of green and efficient oxime ether synthesis methods without the addition of catalysts and additives is still appealing.

Chemical synthesis using visible light as a green energy source has attracted much attention in the past decades.[8] In this regard, the photopromoted functionalization of α-diazo esters though the generation of a free carbene as the key intermediate was first discovered by Davies et al. in 2018[9] and further developed by many other groups.[10,11] As one of most

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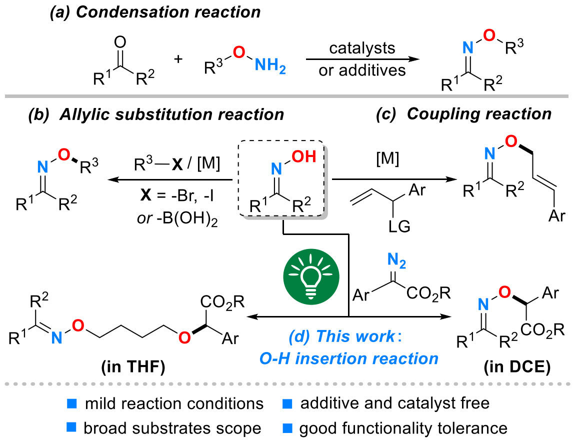
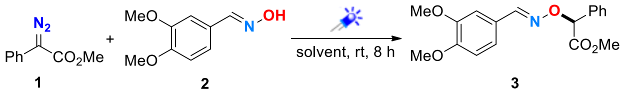
Scheme 2. Methods for the Synthesis of Oxime Ethers



representative reaction activities, insertions of the formed carbene species into the O–H bond of carboxylic acids, phenols, and alcohols have been reported recently.[12] Motivated by those elegant findings, we question whether the photogenerated carbene species from α-diazo esters might also be trapped by oximes, thus providing an alternative method to access oxime ether derivatives (Scheme 2d).[13] Compared with reported oxime ether formation processes, this designed photochemical reaction occurred under green and sustainable reaction conditions without the requirement of any additional catalysts or additives. Herein, we would like to describe the preliminary results of this study.

Initially, methyl 2-diazo-2-phenylacetate **1** and (*E*)-3,4-dimethoxybenzaldehyde oxime **2** were selected as model substrates to optimize the reaction conditions (Table 1). It was found that the desired oxime ether **3** could be obtained in a 61% isolated yield after irradiating the reaction mixture in DCM for 8 h (Table 1, entry 1). Encouraged by this preliminary result, the influence of other reaction media was systematically investigated to further improve the reaction yield. Apart from DCM, CH_3CN and DCE were also suitable for the formation of the desired oxime ether **3**, and DCE was determined as the best reaction medium (Table 1, entries 2 and 3, respectively). In contrast, only a trace amount of oxime ether **3** was detected when the reaction was performed in strong polar solvents, such as DMF and DMSO (Table 1, entries 4 and 5, respectively). To our delight, a three-component coupling product could be obtained when THF was used as the reaction solvent (Table 1, entry 6).[14] Finally, the control experiment revealed that light irradiation was crucial for the formation of the desired oxime ether (Table 1, entry 7).

Table 1. Condition Optimization[a]

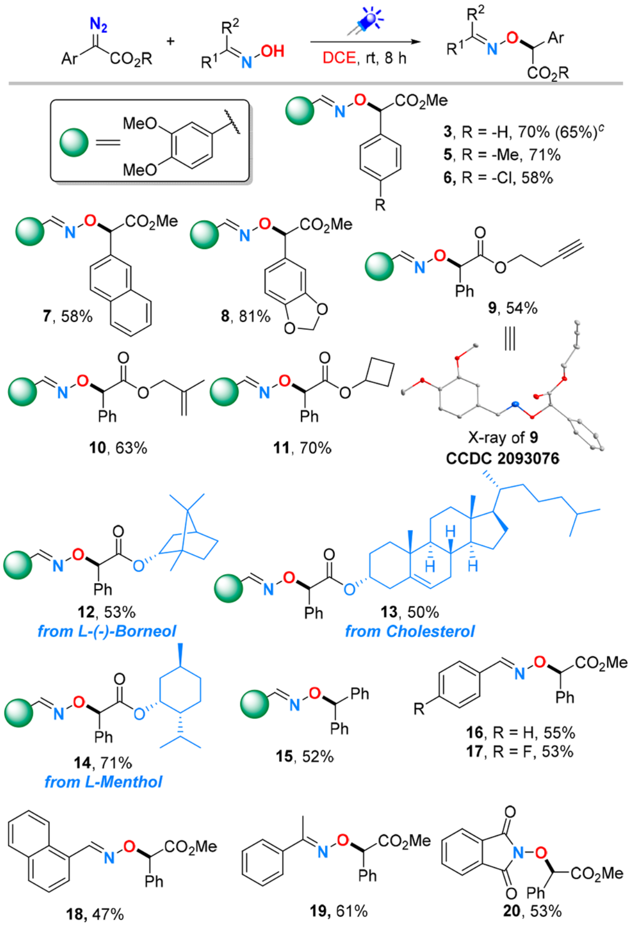


entry	solvent	yield (%)[b]
1	DCM	61
2	CH_3CN	53
3	DCE	70
4	DMSO	trace
5	DMF	trace
6	THF	trace
7[c]	DCE	N.R.

[a] Reaction was performed with **1** (0.6 mmol) and **2** (0.3 mmol) in dry solvent (3.0 mL) at rt under irradiation with 24 W blue LEDs for 8 h. [b] Isolated yield. [c] In dark. N.R. , no reaction.

After the optimal reaction conditions were established, the substrate scope and limitations of the method were subsequently explored. As shown in Table 2, α-diazo esters with different electron-neutral, electron-donating (−Me), or electron-withdrawing (−Cl) substituents at the *para*-position on the phenyl ring were well-tolerated, affording oxime ethers **3**, **5**, and **6**, respectively, in good yields (58−71%). Apart from phenyl diazoacetate, substrates bearing a 2-naphthyl or benzo[*d*][1,3]dioxole moiety were also amenable substrates, and the corresponding oxime ethers **7** and **8** could be isolated in 58% and 81% yields, respectively. Next, we turned our attention to the substituent modification of the ester group in aryldiazoacetates. Replacing a methyl group in the aryldiazoacetates with a cyclic alkyl substituent or alkyl substituents containing sensitive functional groups, such as unsaturated double and triple bonds, successfully produced the corresponding oxime ethers (**9**−**11**) in moderate to good yields (54−70%). Note that the structure of **9** was unambiguously

Table 2. O−H Functionalization of Oximes with α-Diazo Esters in DCE[a,b]



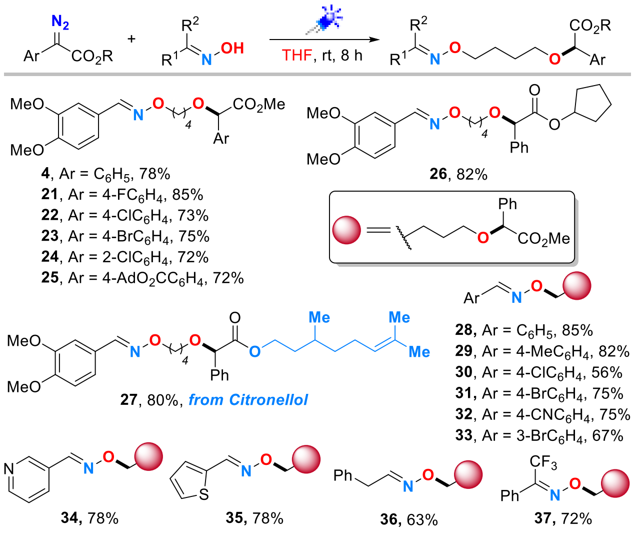
[a] Reaction performed with an α-diazo ester (0.6 mmol) and oxime (0.3 mmol) in dry DCE (3.0 mL) at rt under irradiation with 24 W blue LEDs for 8 h. [b] Isolated yield. [c] Performmed at a 1.0 mmol scale.

confirmed by X-ray diffraction analysis. To further demonstrate the synthetic value this visible-light-promoted oxime ether formation process, we introduced some bioactive complex molecules, such as L-(−)-borneol, cholesterol, and L-menthol, into the structure of aryldiazoacetates. To our delight, the corresponding bioactive complex-molecule-modified oxime ethers could be obtained in good yields (**12**−**14**, 50−71%). In addition, replacing diazo esters with aryl/aryl diazoalkane also proved successful, affording oxime ether **15** in a 52% isolated yield.

Next, we evaluated the scope of the oxime components. Different aryl-substituted aldoximes and acetophenone-derived oximes reacted well under the standard reaction conditions to give the corresponding oxime ethers in moderate to good yields (**16**−**19**). In addition, this O−H insertion reaction can be further extended to modify *N*-hydroxyphthalimide, giving oxime ether **20** in a 53% yield.

As mentioned above, a three-component coupling oxime ether product **4** was obtained in a 78% isolated yield by performing the reaction in THF. Intrigued by this observation, we next studied the scope of different α-diazo esters for this visible-light-promoted three-component oxime ether formation reaction (Table 3). Various halogen-substituted aryldiazoacetates were well-tolerated, leading to oxime ethers (**21**−**24**) in average to good yields (72−85%). When using cyclopentyl and adamantane formic acid-derived aryldiazoacetates, the desired oxime ethers (**25** and **26**, respectively) can be obtained with high efficiencies. The successful introduction of a citronellol fragment into the final oxime ether **27** further disclosed the advantage of this strategy. Then, we turned our attention to examining the scope of the oxime components. Oximes with various electron-rich (−Me,) or electron-deficient (−Cl, −Br, and −CN) groups at *meta*- or *para*- positions of the phenyl ring could be utilized as suitable substrates in the reaction, affording products **28**−**33** in moderate to good yields (56−85%). To our delight, (*E*)-nicotinaldehyde oxime and (*E*)-thiophene-2-carbaldehyde oxime are also suitable substrates apart from phenyl oximes, providing the corresponding products (**34** and **35**) in good yields. Note that aliphatic aldehyde was also a suitable oxime precursor and formed product **36** in a 63% yield. Moreover, when an oxime derived from trifluoroacetophenone was involved, the target trifluoromethyl-containing oxime ether **37** was obtained in a 72% yield.

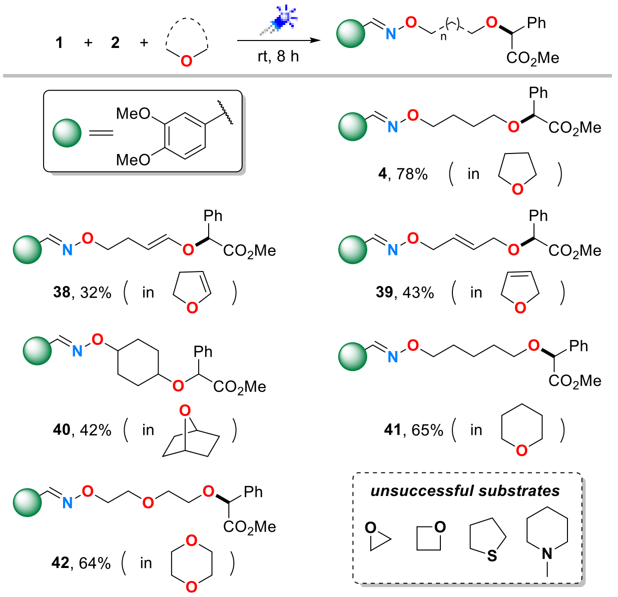
Table 3. O−H Functionalization of Oximes with α-Diazo Esters in THF[a,b]



[a]Reaction performed with an α-diazo ester (0.6 mmol) and oxime (0.3 mmol) in dry THF (3.0 mL) at rt under irradiation with 24 W blue LEDs for 8 h. [b]Isolated yield.

To further show the synthetic potential of this method, we examined the compatibilities of different cyclic ethers (Table 4). As the structural analogues of THF, 2,3-dihydrofuran and 2,5-dihydrofuran reacted smoothly to give oxime ethers **38** and **39**, respectively, in moderate yields. To our delight, the method could be applied to the synthesis of the cyclohexane-tethered oxime ether **40** in a 42% yield by using 7-oxabicyclo[2.2.1]heptane as a carbene trapping reagent. Apart from five-membered cyclic ethers, the replacement of tetrahydrofuran with tetrahydropyran and 1,4-dioxane successfully afforded oxime ethers **41** and **42** in 64% and 65% yields, respectively. We also tested the efficiencies of other cyclic heterocycles, such as ethylene oxide, propylene oxide, tetrahydrothiophene, and *N*-methylpiperidine. Unfortunately, none of those reactions could give the desired three-component coupling products under the optimal conditions. FFor more details about unsuccessful substrates, see the Supporting Information.

Table 4. O−H Functionalization of Oximes with α-Diazo Esters in Other Cyclic Ethers[a,b]



[a]Reaction performed with an α-diazo ester (0.2 mmol) and oxime (0.1 mmol) in cyclic ethers (1.0 mL) at rt under irradiation with 24 W blue LEDs for 8 h. [b]Isolated yield.

We conducted a gram-scale synthesis using the reaction of 2-diazo-2-phenylacetate and benzaldehyde oxime in THF as an example under continuous flow reaction conditions (Section 6 in the Supporting Information). After 8 h of irradiation in a continuous flow, oxime ether **28** still could be isolated in an 83% yield.

Based on the literature reports,[10−12] a plausible reaction mechanism was proposed to explain the oxime ether formation process (Section 7 in the Supporting Information). Under irradiation with a blue LED, the photolysis of α-diazo esters gives the carbene intermediate **A**. The insertion of **A** into the O−H bond of an oxime afforded the corresponding oxime ether when the reaction was performed in DCE (path A).[12] In THF, trapping the carbene species **A** with the solvent delivered the ylide intermediate **B**.[10,11f] Then, the protonation of **B**, followed by the ring opening of **C**, furnished the final three-component coupling product (path B).

In summary, we have developed a visible-light-promoted O−H functionalization of oximes with diazo esters for the synthesis of oxime ether derivatives. In contrast to conventional methods, the reaction described herein proceeded under extremely mild conditions without any additional additives and catalysts. An interesting three-component coupling product was observed when the reaction was performed in THF. The broad substrate scope, excellent functional group tolerance, and large-scale preparation in continuous flow conditions further documented the synthetic potential of this methodology.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c02555.

Experimental procedures, characterization data, and ^{1}H and ^{13}C NMR spectra (PDF)

Accession Codes

CCDC 2093076 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 Author

Jun Xuan − *Anhui Province Key Laboratory of Chemistry for Inorganic/Organic Hybrid Functionalized Materials, College of Chemistry & Chemical Engineering, Anhui University, Hefei, Anhui 230601, People's Republic of China; Key Laboratory of Structure and Functional Regulation of Hybrid Materials, Ministry of Education, Anhui University, Hefei 230601, People's Republic of China; Key Laboratory of Precise Synthesis of Functional Molecules of Zhejiang Province, School of Science, Westlake University, Hangzhou 310024 Zhejiang Province, China*; orcid.org/0000-0003-0578-9330; Email: xuanjun@ahu.edu.cn

Authors

Qian Li − *Anhui Province Key Laboratory of Chemistry for Inorganic/Organic Hybrid Functionalized Materials, College of Chemistry & Chemical Engineering, Anhui University, Hefei, Anhui 230601, People's Republic of China*

Bao-Gui Cai − *Anhui Province Key Laboratory of Chemistry for Inorganic/Organic Hybrid Functionalized Materials, College of Chemistry & Chemical Engineering, Anhui University, Hefei, Anhui 230601, People's Republic of China*

Lei Li − *Anhui Province Key Laboratory of Chemistry for Inorganic/Organic Hybrid Functionalized Materials, College of Chemistry & Chemical Engineering, Anhui University, Hefei, Anhui 230601, People's Republic of China*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.1c02555

Notes

The authors declare no competing financial interest.

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REFERENCES

(1) (a) Itsuno, S.; Matsumoto, T.; Sato, D.; Inoue, T. Enantioselective reduction of oxime ethers with borane catalyzed by polymer-supported 2-piperazinemethanol. *J. Org. Chem.* **2000**, *65*, 5879−5881. (b) Tillyer, R. D.; Boudreau, C.; Tschaen, D.; Dolling, U.-H.; Reider, P. J. Asymmetric reduction of keto oxime ethers using oxazaborolidine reagents. The enantioselective synthesis of cyclic amino alcohols. *Tetrahedron Lett.* **1995**, *36*, 4337−4340. (c) Moody, C. J.; Gallagher, P. T.; Lightfoot, A. P.; Slawin, A. M. Z. Chiral oxime ethers in asymmetric synthesis. 3. asymmetric synthesis of (*R*)-N-protected α-amino acids by the addition of organometallic reagents to the ROPHy oxime of cinnamaldehyde. *J. Org. Chem.* **1999**, *64*, 4419−4425. (d) Li, X.-T.; Gu, Q.-S.; Dong, X.-Y.; Meng, X.; Liu, X.-Y. A copper catalyst with a cinchona-alkaloid-based sulfonamide ligand for asymmetric radical oxytrifluoromethylation of alkenyl oximes. *Angew. Chem., Int. Ed.* **2018**, *57*, 7668−7672. (e) Rong, B.; Xu, G.; Yan, H.; Zhang, S.; Wu, Q.; Zhu, N.; Duan, J.; Guo, K. The copper-catalyzed synthesis of dihydrooxazoles from *α,β*-unsaturated ketoximes and activated ketones. *Chem. Commun.* **2021**, *57*, 7272−7275.

(2) (a) van Hoogdalem, E.J; van den Hoven, W.E; Terpstra, I.J; van Zijtveld, J; Verschoor, J.S.C; Visser, J.N Nail penetration of the antifungal agent oxiconazole after repeated topical application in healthy volunteers, and the effect of acetylcysteine. *Eur. J. Pharm. Sci.* **1997**, *5*, 119−127. (b) Jegasothy, B.; Pakes, G. Oxiconazole nitrate: Pharmacology, efficacy, and safety of a new imidazole antifungal agent. *Clin. Ther.* **1991**, *13*, 126−141. (c) Torano, J. S.; Guchelaar, H.-J. Quantitative determination of the macrolide antibiotics erythromycin, roxithromycin, azithromycin and clarithromycin in human serum by high-performance liquid chromatography using pre-column derivatization with 9-fluorenylmethyloxycarbonyl chloride and fluorescence detection. *J. Chromatogr., Biomed. Appl.* **1998**, *720* (89−97), 121−127. (d) Perse, T. L.; Greist, J. H.; Jefferson, J. W.; Rosenfeld, R.; Dar, R. Fluvoxamine treatment of obsessive-compulsive disorder. *Am. J. Psychiatry* **1987**, *144*, 1543−1548. (e) Apter, A.; Ratzoni, G.; King, R. A.; Weizman, A.; Iancu, I.; Binder, M.; Riddle, M. A. Fluvoxamine open-label treatment of adolescent inpatients with obsessive-compulsive disorder or depression. *J. Am. Acad. Child. Adolesc. Psychiatry.* **1994**, *33*, 342−348. (f) Motoba, K.; Nishizawa, H.; Suzuki, T.; Hamaguchi, H.; Uchida, M.; Funayama, S. Species-specific detoxification metabolism of Fenpyroximate, a potent acaricide. *Pestic. Biochem. Physiol.* **2000**, *67*, 73−84. (g) Al-Rahman, S. H. A.; Almaz, M.; Osama, I. Determination of degradation rate of acaricide Fenpyroximate in apple, citrus, and grape by HPLC-DAD. *Food. Anal. Method.* **2012**, *5*, 306−311.

(3) (a) Zard, S. Z. Recent progress in the generation and use of nitrogen-centred radicals. *Chem. Soc. Rev.* **2008**, *37*, 1603−1618. (b) Li, J.; Hu, Y.; Zhang, D.; Liu, Q.; Dong, Y.; Liu, H. Transition metal-catalyzed reactions involving oximes. *Adv. Synth. Catal.* **2017**, *359*, 710−771. (c) Chen, C.; Zhao, J.; Shi, X.; Liu, L.; Zhu, Y.-P.; Sun, W.; Zhu, B. Recent advances in cyclization reactions of unsaturated oxime esters (ethers): synthesis of versatile functionalized nitrogen-containing scaffolds. *Org. Chem. Front.* **2020**, *7*, 1948−1969. (d) Yu, X.-Y.; Chen, J.-R.; Xiao, W.-J. Visible light-driven radical-mediated C−C bond cleavage/functionalization in organic synthesis. *Chem. Rev.* **2021**, *121*, 506−561. (e) Murakami, M.; Ishida, N. Cleavage of carbon−carbon σ-bonds of four-membered rings. *Chem. Rev.* **2021**, *121*, 264−299.

(4) (a) Li, C.- B.; Zhang, H.; Cui, Y.; Zhang, S.-M.; Zhao, Z.-Y.; Choi, M. C. K.; Chan, A. S. C. One-pot synthesis of oxime ethers

from benzaldehyde or acetophenone, hydroxylamine salt, potassium hydroxide, and alkyl halides. *Synth. Commun.* **2003**, *33*, 543−546. (b) Takeda, N.; Miyata, O.; Naito, T. Efficient synthesis of benzofurans utilizing [3,3]-sigmatropic rearrangement triggered by N-trifluoroacetylation of oxime ethers: short synthesis of natural 2-arylbenzofurans. *Eur. J. Org. Chem.* **2007**, *2007*, 1491−1509. (c) Nimmagadda, S. K.; Mallojjala, S. C.; Woztas, L.; Wheeler, S. E.; Antilla, J. C. Enantioselective synthesis of chiral oxime ethers: desymmetrization and dynamic kinetic resolution of substituted cyclohexanones. *Angew. Chem., Int. Ed.* **2017**, *56*, 2454−2458.

(5) (a) De, P.; Nonappa; Pandurangan, K.; Maitra, U.; Wailes, S. CuI-Mediated cross-coupling of aryl halides with oximes: a direct access to O-aryloximes. *Org. Lett.* **2007**, *9*, 2767−2770. (b) Maimone, T. J.; Buchwald, S. L. Pd-Catalyzed O-arylation of ethyl acetohydroximate: synthesis of O-arylhydroxylamines and substituted benzofurans. *J. Am. Chem. Soc.* **2010**, *132*, 9990−9991. (c) Reeta; Rangarajan, T. M.; Singh, R. P.; Singh, R. P.; Singh, M. An easy access to oxime ethers by Pd-catalyzed C-O cross-coupling of activated aryl bromides with ketoximes and chalcone oximes. *Chin. J. Chem.* **2020**, *38*, 830−836.

(6) (a) Feng, X.-H.; Zhang, G.-Z.; Chen, C.; Yang, M.-Y.; Xu, X.-Y.; Huang, G.-S. Copper(II) acetate−mediated cross-coupling of phenylboronic acids with aryloximes: synthesis of O-aryloximes. *Synth. Commun.* **2009**, *39*, 1768−1780. (b) Wang, L.; Huang, C.-Y.; Cai, C. Polymer-supported copper complex for the direct synthesis of O-aryloxime ethers via cross-coupling of oximes and arylboronic acids. *Catal. Commun.* **2010**, *11*, 532−536.

(7) (a) Miyabe, H.; Matsumura, A.; Moriyama, K.; Takemoto, Y. Utility of the iridium complex of the pybox ligand in regio- and enantioselective allylic substitution. *Org. Lett.* **2004**, *6*, 4631−4634. (b) Miyabe, H.; Yoshida, K.; Reddy, V. K.; Matsumura, A.; Takemoto, Y. Selective synthesis of allylated oxime ethers and nitrones based on palladium-catalyzed allylic substitution of oximes. *J. Org. Chem.* **2005**, *70*, 5630−5635. (c) Jin, J.; Li, Y.; Wang, Z.-J.; Qian, W.-X.; Bao, W.-L. A concise, metal-free approach to the synthesis of oxime ethers from cross-dehydrogenative-coupling of sp^3 C−H bonds with oximes. *Eur. J. Org. Chem.* **2010**, *2010*, 1235−1238.

(8) (a) Narayanam, J. M. R.; Stephenson, C. R. J. Visible light photoredox catalysis: applications in organic synthesis. *Chem. Soc. Rev.* **2011**, *40*, 102−113. (b) Xuan, J.; Xiao, W.-J. Visible-light photoredox catalysis. *Angew. Chem., Int. Ed.* **2012**, *51*, 6828−6838. (c) 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. (d) Hopkinson, M. N.; Sahoo, B.; Li, J.-L.; Glorius, F. Dual catalysis sees the light: combining photoredox with organo-, acid, and transition-metal catalysis. *Chem. - Eur. J.* **2014**, *20*, 3874−3886. (e) Marzo, L.; Pagire, S.; Reiser, O.; König, B. Visible-light photocatalysis: does it make a difference in organic synthesis? *Angew. Chem., Int. Ed.* **2018**, *57*, 10034−10072. (f) Chen, Y.; Lu, L.-Q.; Yu, D.-G.; Zhu, C.-J.; Xiao, W.-J. Visible light-driven organic photochemical synthesis in China. *Sci. China: Chem.* **2019**, *62*, 24−57. (g) Cai, B.-G.; Xuan, J.; Xiao, W.-J. Visible light-mediated C-P bond formation reactions. *Sci. Bull.* **2019**, *64*, 337−350. (h) Xuan, J.; He, X.-K.; Xiao, W.-J. Visible light-promoted ring-opening functionalization of three-membered carbo- and heterocycles. *Chem. Soc. Rev.* **2020**, *49*, 2546−2556.

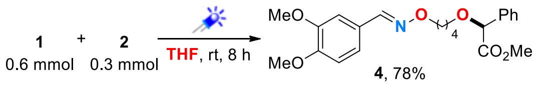
(9) Jurberg, I.; Davies, H. M. L. Blue light-promoted photolysis of aryldiazoacetates. *Chem. Sci.* **2018**, *9*, 5112−5118.

(10) (a) Ciszewski, L. W.; Rybicka-Jasinska, K.; Gryko, D. Recent developments in photochemical reactions of diazo compounds. *Org. Biomol. Chem.* **2019**, *17*, 432−448. (b) Yang, Z.; Stivanin, M. L.; Jurberg, I. D.; Koenigs, R. M. Visible light-promoted reactions with diazo compounds: a mild and practical strategy towards free carbene intermediates. *Chem. Soc. Rev.* **2020**, *49*, 6833−6847. (c) Jana, S.; Guo, Y.; Koenigs, R. M. Recent perspectives on rearrangement reactions of ylides via carbene transfer reactions. *Chem. - Eur. J.* **2021**, *27*, 1270−1281.

(11) (a) Xiao, T.; Mei, M.; He, Y.; Zhou, L. Blue light-promoted cross-coupling of aryldiazoacetates and diazocarbonyl compounds. *Chem. Commun.* **2018**, *54*, 8865−8868. (b) Yang, J.; Wang, J.; Huang, H.; Qin, G.; Jiang, Y.; Xiao, T. *gem*-difluoroallylation of aryl diazoesters via catalyst-free, blue-light-mediated formal Doyle−Kirmse reaction. *Org. Lett.* **2019**, *21*, 2654−2657. (c) Hommelsheim, R.; Guo, Y.; Yang, Z.; Empel, C.; Koenigs, R. M. Blue-light-induced carbene-transfer reactions of diazoalkanes. *Angew. Chem., Int. Ed.* **2019**, *58*, 1203−1207. (d) Jana, S.; Yang, Z.; Pei, C.; Xu, X.; Koenigs, R. M. Photochemical ring expansion reactions: synthesis of tetrahydrofuran derivatives and mechanism studies. *Chem. Sci.* **2019**, *10*, 10129−10134. (e) Orłowska, K.; Rybicka-Jasińska, K.; Krajewski, P.; Gryko, D. Photochemical Doyle−Kirmse reaction: a route to allenes. *Org. Lett.* **2020**, *22*, 1018−1021. (f) He, F.; Pei, C.; Koenigs, R. M. Photochemical fluoro-amino etherification reactions of aryldiazoacetates with NFSI under stoichiometric conditions. *Chem. Commun.* **2020**, *56*, 599−602. (g) Cheng, R.; Qi, C.; Wang, L.; Xiong, W.; Liu, H.; Jiang, H. Visible light-promoted synthesis of organic carbamates from carbon dioxide under catalyst-and additive-free conditions. *Green Chem.* **2020**, *22*, 4890−4895. (h) Cai, B.-G.; Luo, S.-S.; Li, L.; Li, L.; Xuan, J.; Xiao, W.-J. Visible light-promoted amide bond formation *via* one-pot nitrone *in situ* formation/rearrangement cascade. *CCS Chem.* **2020**, *2*, 2764−2771. (i) Cheng, X.; Cai, B.-G.; Mao, H.; Lu, J.; Li, L.; Wang, K.; Xuan, J. Divergent synthesis of aziridine and imidazolidine frameworks under blue LED irradiation. *Org. Lett.* **2021**, *23*, 4109−4114. (j) Lu, J.; Li, L.; He, X.-K.; Xu, G.-Y.; Xuan, J. Visible light-promoted sulfoxonium ylides synthesis from aryl diazoacetates and sulfoxides. *Chin. J. Chem.* **2021**, *39*, 1646−1650. (k) Ye, C.; Cai, B.-G.; Lu, J.; Cheng, X.; Li, L.; Pan, Z.-W.; Xuan, J. Visible-light-promoted polysubstituted olefins synthesis involving sulfur ylides as carbene trapping reagents. *J. Org. Chem.* **2021**, *86*, 1012−1022.

(12) (a) He, F.; Koenigs, R. M. Visible light mediated, metal-free carbene transfer reactions of diazoalkanes with propargylic alcohols. *Chem. Commun.* **2019**, *55*, 4881−4884. (b) Guo, Y.; Nguyen, T. V.; Koenigs, R. M. Norcaradiene synthesis via visible-light-mediated cyclopropanation reactions of arenes. *Org. Lett.* **2019**, *21*, 8814−8818. (c) Jana, S.; Yang, Z.; Li, F.; Empel, C.; Ho, J.; Koenigs, R. M. Photoinduced proton-transfer reactions for mild O-H functionalization of unreactive alcohols. *Angew. Chem., Int. Ed.* **2020**, *59*, 5562−5566. (d) Yang, J.; Wang, G.; Zhou, H.; Li, Z.; Ma, B.; Song, M.; Sun, R.; Huo, C. Visible-light-promoted selective *O*-alkylation of 2-pyridones with α-aryldiazoacetates. *Org. Biomol. Chem.* **2021**, *19*, 394−398. (e) Zhou, S.-J.; Cai, B.-G.; Hu, C.-X.; Cheng, X.; Li, L.; Xuan, J. Visible light and base promoted O-H insertion/cyclization of *para*-quinone methides with aryl diazoacetates: An approach to 2,3-dihydrobenzofuran derivatives. *Chin. Chem. Lett.* **2021**, DOI: 10.1016/j.cclet.2021.03.010.

(13) During the preparation of this manuscript, Huang and coworkers reported a CF_3SO_3H-catalyzed reaction of oximes with α-diazo esters, see: Zhang, Z.; He, Z.; Xie, Y.; He, T.; Fu, Y.; Yu, Y.; Huang, F. Brønsted acid-catalyzed homogeneous O−H and S−H insertion reactions under metal- and ligand-free conditions. *Org. Chem. Front.* **2021**, *8*, 1233−1242.



(14) The three-component coupling product **4** could be obtained in a 78% isolated yield by using THF as the reaction solvent.