OL | Organic Letters

pubs.acs.org/OrgLett Letter

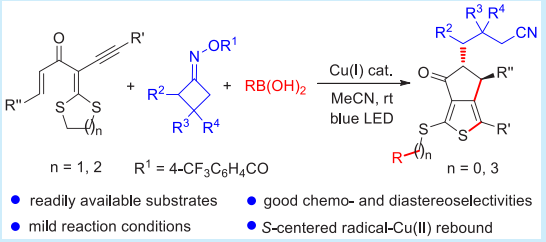
Photoinduced, Copper-Catalyzed Three-Component Annulation of *gem*-Dialkylthio Enynes

Jiang Lou, Juan Ma, Bao-Hua Xu, Yong-Gui Zhou,* and Zhengkun Yu*

Cite This: *Org. Lett.* 2020, 22, 5202–5206 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: Photoinduced, copper-catalyzed three-component radical annulation of *gem*-dialkylthio enynes, cyclobutanone oxime esters, and boronic acids was achieved, forming highly functionalized aryl thienyl sulfides with both good chemo- and diastereoselectivities. The reaction proceeds through a domino sequence involving cyanoalkyl radical-mediated intramolecular annulation of *gem*-dialkylthio enyne, alkenyl radical-promoted C(sp^3)−S bond cleavage, and sulfur-centered radical-trapped Cu(II)-facilitated C−S cross-coupling. The protocol features simultaneous establishment of cyanoalkyl, cyclopentanone, and thiophene moieties and a thioether C−S bond in one pot with broad substrate scopes and versatile functional group tolerance under mild conditions.



Aryl-2-thienyl sulfides are among the important skeletons in pharmaceutical compounds and functional materials.[1] For example, AZD4407 is used as an antiallergic/antiasthmatic agent for chronic obstructive pulmonary diseases,[2] CCT365623 significantly reduces the tumor growth,[3] and bis(arylthio)oligothiophenes exhibit better electronic properties than unsubstituted oligothiophenes (Figure 1).[4] Many

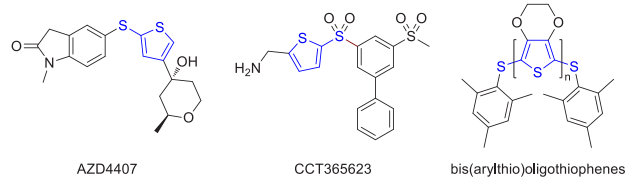


Figure 1. Representative examples of aryl-2-thienyl sulfides used in pharmaceuticals and functional materials.

efforts have been devoted to the synthesis of functionalized aryl-2-thienyl sulfides.[5] In this regard, radical cyclization of unsaturated carbon−carbon bonds with sulfur-centered radicals has been well documented.[6] However, use of toxic and unstable reagents, employing prefunctionalized substrates, and the poisoning effect on transition metals by sulfur compounds limit the application of these synthetic methods. In this area, efficient protocols for the construction of a thiophene ring and thioether C−S bonds in one pot under mild conditions from readily available and bench-stable substrates have been seldom explored.[7]

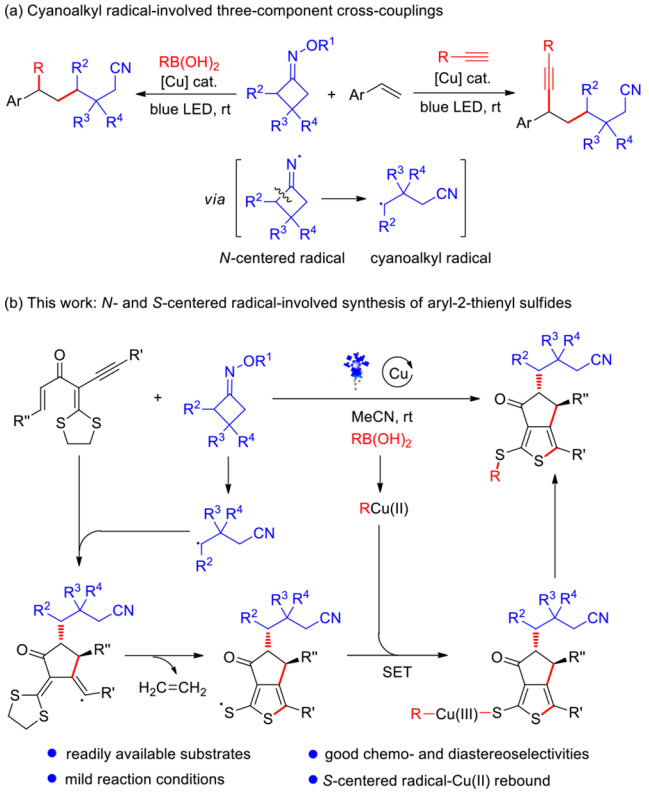
Transition-metal-catalyzed radical cross-coupling reactions have recently received much attention for the construction of complex compounds.[8] In this regard, cyanoalkyl radicals[9] generated from the nitrogen-centered radicals via β-C−C bond cleavage of cycloketone oxime esters and analogs under various conditions can be utilized to couple with unsaturated compounds to achieve cyanoalkylation.[10] However, multicomponent radical cross-couplings involving cyanoalkyl radicals under mild conditions have received much less attention. Xiao and Chen et al. disclosed visible-light-driven, copper-catalyzed three-component radical cross-couplings between oxime esters, styrenes, and boronic acids or terminal alkynes to access 1,1-diarylmethane-based alkylnitriles[11a] and cyanoalkyl-containing propargylic compounds,[11b] respectively (Scheme 1a). Mechanistic studies have suggested that a radical-Cu(II) rebound process involving the benzylic radical intermediate generated from addition of a cyanoalkyl radical to styrene is the key step to execute the radical cross-coupling reaction. In this context, sulfur-centered radical-Cu(II) rebound processes remain unknown due to the intrinsic instability and catalyst-poisoning of a sulfur radical to interfere with the catalyst turnover.[12]

During the continuous investigation of transition-metal-catalyzed annulation of *gem*-dialkylthio internal alkenes, we found that they were usually involved in production of *O*- and *S*-heterocycles.[7a,13] Wang and Liu et al. reported the benzannulation of α-alkynyl-α-alkenoyl ketene dithioacetals with cyanoacetates to form benzo[*b*]thiophenes.[14] Thus, we envisioned that α-alkynyl-α-oxo ketene dithioacetals, that is, *gem*-dialkylthio 1,3-enynes, might be employed for discrete thiophene ring construction under transition-metal catalysis.

Received: May 31, 2020
Published: June 19, 2020

https://dx.doi.org/10.1021/acs.orglett.0c01645
Org. Lett. 2020, 22, 5202−5206

Scheme 1. *N*- and *S*-Centered Radical Multicomponent Cross-Couplings

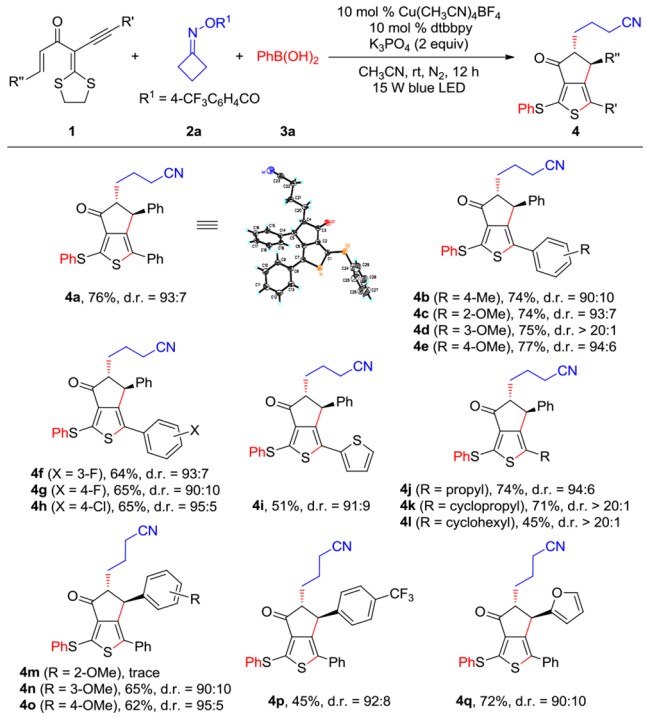


With the following concept in mind, a three-component annulation process is designed as shown in Scheme 1b. The cyanoalkyl radical generated *in situ* from the initially formed *N*-centered radical interacts with the *gem*-dialkylthio 1,3-enyne substrate to initiate the annulation cascade, forming an alkenyl radical with construction of the five-membered carbocycle. Subsequent electrophilic attack of one of the sulfur atoms at the radical carbon establishes a discrete thiophene ring with release of ethylene by C(sp^3)−S bond cleavage and generation of the sulfur-centered radical which is then coupled by a boronic acid, giving the target product under photoinduced copper catalysis. Herein, we report such a three-component process for the synthesis of aryl-2-thienyl sulfides.

Initially, the reaction of *gem*-dialkylthio enyne **1a**, cyclobutanone oxime ester (**2a**), and phenylboronic acid (**3a**) was conducted to screen the reaction conditions (see the Supporting Information for details). After the systematic work, the optimal reaction conditions were identified. In the presence of 10 mol % $Cu(CH_3CN)_4BF_4$, 10 mol % dtbbpy, and K_3PO_4 (2 equiv) in CH_3CN under the irradiation of a 15 W blue LED at ambient temperature, the reaction gave the target product **4a** in 76% isolated yield and a diastereoselectivity of 93/7, and **4a** could be obtained in 70% yield on a 2 mmol scale of **1a**. Both $CuCl_2$ and CuCl also promoted the reaction, but the nickel(II) catalyst $NiCl_2$·glyme was not effective. Use of other ligands such as 2,2′-bpy and 1,10-phen, bases Na_2CO_3 and K_2CO_3, and acetone and EtOAc as the solvents, diminished the reaction efficiency. The control experiments revealed that the $Cu(CH_3CN)_4BF_4$ catalyst, dtbbpy ligand, and K_3PO_4 base were crucial for the reaction. Notably, the reaction only afforded **4a** in 50% yield without the visible-light irradiation.

Under the optimal conditions, the scope of *gem*-dialkylthio enynes (**1**) was investigated by reacting with **2a** and **3a** (Scheme 2). Introduction of an electron-donating group such

Scheme 2. Scope of *gem*-Dialkylthio Enynes (1)[a]



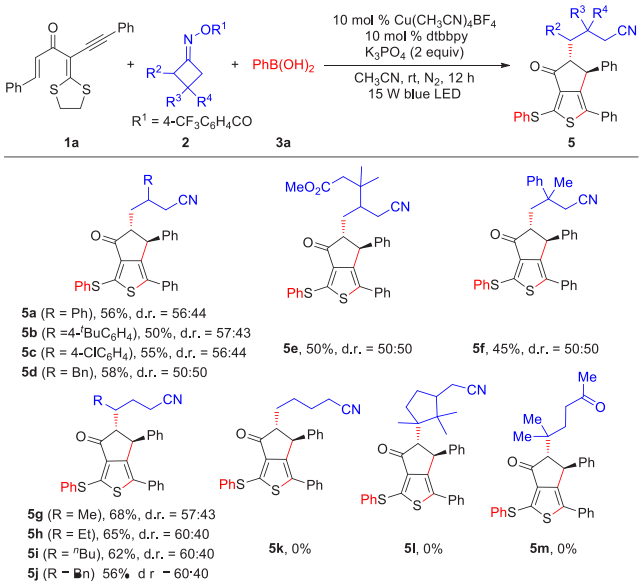
[a]Conditions: **1** (0.2 mmol), **2a** (0.4 mmol), **3a** (0.4 mmol), $Cu(CH_3CN)_4BF_4$ (10 mol %), dtbbpy (10 mol %), K_3PO_4 (0.4 mmol), CH_3CN (2 mL), rt, 0.1 MPa N_2, irradiation using a 15 W blue LED, 12 h.

as methyl or methoxy to the terminal aryl functionality attached to the alkynyl backbone of enyne **1** resulted in no obvious impact on the formation of the target products **4a**−**4e** (74−77%) with a diastereoselectivity of 90/10 to 20/1, while electron-withdrawing fluoro and chloro substituents diminished the yields of products **4f**−**4h** (64−65%). 2-Thienyl also exhibited a negative effect on the reaction efficiency, leading to **4i** in 51% yield. A terminal propyl or cyclopropyl did not affect the formation of **4j** (74%) and **4k** (71%). As the steric hindrance of the terminal alkyl increased, cyclohexyl obviously deteriorated the formation of **4l** (45%), but with a high diastereoselectivity (>20:1). The steric effect from the alkenoyl moiety of enynes **1** was remarkable. 2-Methoxyphenyl inhibited the formation of compound **4m** due to the increased steric hindrance, whereas 3- and 4-methoxyphenyl, 4-trifluoromethylphenyl, and 2-furyl-functionalized alkenoyl based enynes reacted well to give the target products **4n**−**4q** (45−72%) with high diastereoselectivities. These results have suggested that the reaction is highly dependent on the electronic and steric effects from the functionalities at the terminuses of the alkynyl and alkenoyl moieties of substrates **1**. It is noteworthy that the molecular structure of compound **4a** was further confirmed by the X-ray single crystal crystallographic determination (see the Supporting Information for details).

Next, the protocol generality was explored by performing the reaction of **1a** and **3a** with a variety of cycloketone oxime esters (**2**) under the standard conditions (Scheme 3). 3-Phenyl

https://dx.doi.org/10.1021/acs.orglett.0c01645
Org. Lett. 2020, 22, 5202−5206

Scheme 3. Scope of Cycloketone Oxime Esters (2)[a]

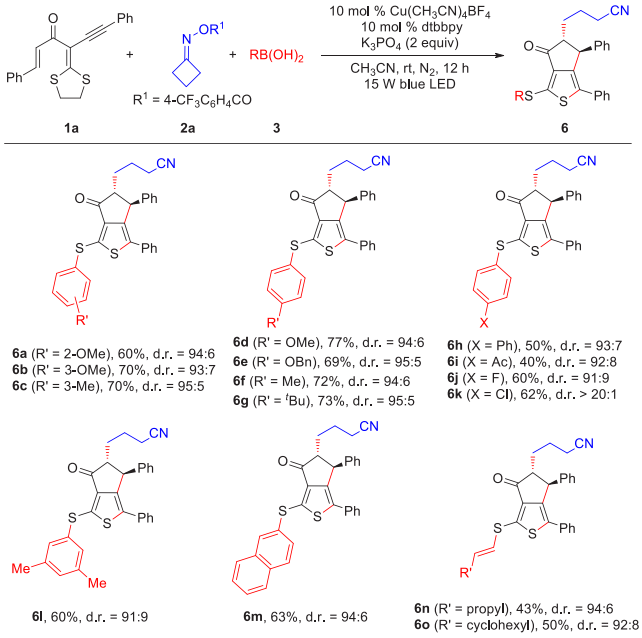


[a]Conditions: **1a** (0.2 mmol), **2** (0.4 mmol), **3a** (0.4 mmol), $Cu(CH_3CN)_4BF_4$ (10 mol %), dtbbpy (10 mol %), K_3PO_4 (0.4 mmol), CH_3CN (2 mL), rt, 0.1 MPa N_2, irradiation using a 15 W blue LED, 12 h.

substituted cyclobutanone oxime ester (**2b**) underwent the reaction smoothly to give the target product **5a** in 56% yield with d.r. = 56/44. 3-(4-*tert*-Butyl) and 3-(4-chloro)-substituted phenyl, 3-benzyl, and 3-alkyl-bearing cyclobutanone oxime esters reacted similarly to form **5b**−**5e** (50−58%), respectively. Increased steric hindrance led to lowered yields for **5b** (50%) and **5e** (50%). 3-Methyl-3-phenyl disubstituted oxime ester (**2g**) further increased the steric hindrance to execute the formation of **5f** in a moderate yield (45%). However, 2-alkyl substituents such as methyl, ethyl, and butyl in **2** enhanced the yields of products **5g**−**5i** to 62−68% in comparison to the 3-substituent-bearing cases, which is attributed to the stabilization of 2-alkyls to the *in situ* generated cyanoalkyl radicals that initiate the annulation process. 2-Benzyl exhibited a negative steric effect on the formation of **5j** (56%). It should be noted that cyclopentanone- and cyclohexanone-derived oxime esters **2l** and **2m** and the corresponding acyclic oxime ester of 5-methyl-2-hexanone (**2n**) could not undergo the same type of radical cross-coupling reactions under the stated conditions, and the desired products **5k**−**5m** were not produced.

Finally, the scope of boronic acids (**3**) was extended by treating them with **1a** and **2a** (Scheme 4). Obvious steric and electronic effects were observed from arylboronic acids. The electron-donating substituents such as methoxy, methyl, benzyloxy, and *tert*-butyl facilitated the reaction to form the target products **6a**−**6g** (60−77%) with diastereoselectivity from 93/7 to 95/5, while the phenyl group and electron-withdrawing substituents acetyl, fluoro, and chloro reduced the yields of products **6h**−**6k** (40−62%). The steric effect was obvious in the cases of using 2- methoxy and 3,5-dimethylphenylboronic acids and 2-naphthyl boronic acid, leading to **6a** (60%), **6l** (60%), and **6m** (63%), respectively, as compared with the formation of **6b** (70%)/**6d** (77%), **6c** (70%), and **4a** (76%). It is noteworthy that vinylboronic acids such as 1-pentenyl and 2-cyclohexylvinyl boronic acids also effectively participated in the reaction, affording products **6n**

Scheme 4. Scope of Boronic Acids (3)[a]

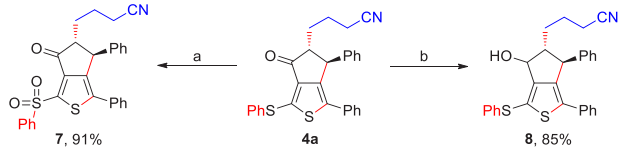


[a]Conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), **3** (0.4 mmol), $Cu(CH_3CN)_4BF_4$ (10 mol %), dtbbpy (10 mol %), K_3PO_4 (0.4 mmol), CH_3CN (2 mL), rt, 0.1 MPa N_2, irradiation using a 15 W blue LED, 12 h.

and **6o** in moderate yields (43−50%) with tolerance of a carbon−carbon double bond under the stated conditions. However, heteroaryl boronic acids such as 2-thienyl and 2-furyl boronic acids only reacted to afford trace amounts of the target products, and 2-alkylboronic acids could not react under the same conditions.

To demonstrate the applicability of the synthetic protocol, various transformations of product **4a** were performed (Scheme 5). With *m*-chloroperoxybenzoic acid (*m*-CPBA) as

Scheme 5. Derivatizations of Thiophene Product 4a[a]



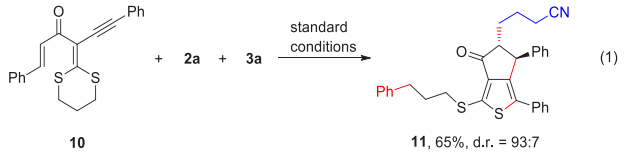
[a]Conditions: (a) **4a** (0.2 mmol), *m*-CPBA (0.6 mmol), CH_2Cl_2 (2 mL), rt, 1.5 h; (b) **4a** (0.2 mmol), $NaBH_4$ (0.2 mmol), MeOH (2 mL), rt, 10 h.

the oxidant **4a** was readily converted to the corresponding sulfone **7** (91%) through oxidation of the phenylthio group. The ketone carbonyl of **4a** was selectively reduced to hydroxyl (85%) by means of $NaBH_4$ as the reductant with the tolerance of a cyano group.

Control experiments were conducted to probe into the reaction mechanism. Addition of 2 equiv of a radical scavenger, that is, 2,6-di-*tert*-butyl-4-methylphenol (BHT), into the reaction system of **1a**, **2a**, and **3a** under the standard conditions obviously diminished the yield of **4a** to 32%, while use of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) completely inhibited the reaction. The radical-trapping product TEMPO-$(CH_2)_3CN$ (**9**) was detected in the reaction mixture

https://dx.doi.org/10.1021/acs.orglett.0c01645
Org. Lett. 2020, 22, 5202−5206

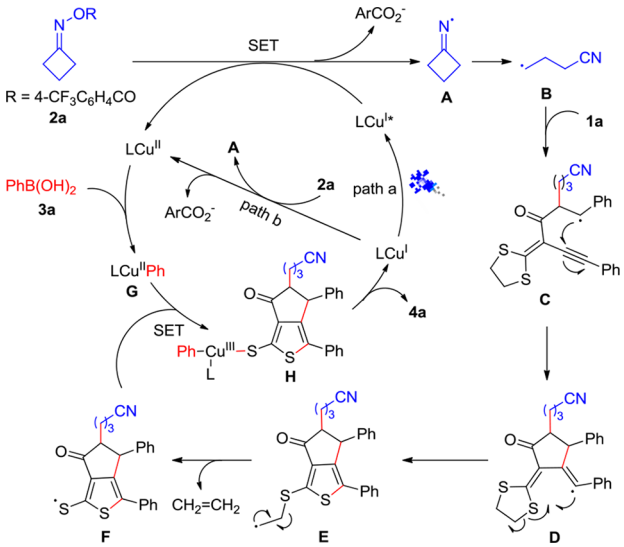
by HRMS analysis (see the Supporting Information for details). These results have implicated that the reaction may proceed through a radical pathway. To identify the possible redox states of the copper catalyst that might be involved in the process, EPR spectroscopy was employed to investigate the redox process between $Cu(CH_3CN)_4BF_4$/dtbbpy or $Cu(CH_3CN)_4BF_4$/dtbbpy/**1a** with cyclobutanone oxime ester (**2a**). Addition of **2a** to the solution of $Cu(CH_3CN)_4BF_6$/dtbbpy or $Cu(CH_3CN)_4BF_4$/dtbbpy/**1a** in CH_3CN resulted in obvious EPR signals of a Cu(II) species (see the Supporting Information for details).[11,15] These results suggest a single-electron transfer (SET) process between the Cu(I) complex and substrate **2a**. To validate that the C(sp^3)−S bond cleavage was facilitated by the *in situ* generated alkenyl radical and the resultant Cu(II) species was trapped by the *in situ* generated *S*-centered radical, six-membered *gem*-dialkylthio enyne **10** was reacted with **2a** and **3a** under the standard conditions (eq 1).



The three-component radical cross-coupling reaction occurred to afford product **11** (65%) with retention of the $(CH_2)_3$ group of the dialkylthio moiety of **10**, suggesting involvement of a carbon-centered radical-Cu(II) rebound process without β-H elimination.

On the basis of these results and the known reports,[9−12] a plausible mechanism is proposed in Scheme 6. Initially,

Scheme 6. Proposed Mechanism



interaction of cyclobutanone oxime ester **2a** with photoexcited complex LCu^{I}* (*path a*) or the ground state complex LCu^{I} (*path b*) via a SET process generated iminyl (*N*-centered) radical **A** and the oxidized LCu^{II} species. Iminyl radical **A** undergoes homolytic α,β-C−C cleavage to form γ-cyanoalkyl radical **B**, which is captured by *gem*-dialkylthio 1,3-enyne **1a** to yield a relatively stable alkyl radical **C**, followed by intramolecular cyclization to form alkenyl radical species **D**. The alkenyl radical facilitates the homolytic C(sp^3)−S bond cleavage to produce alkyl radical species **E**, which releases a molecule of ethylene to form sulfur-centered radical **F**. Subsequently, radical **F** is intercepted by the $LCu^{II}Ph$ complex generated *in situ* from the transmetalation between LCu^{II} species and boronic acid $PhB(OH)_2$ (**3a**), yielding high-valent Cu^{III} species **H**, which undergoes reductive elimination to give the target product **4a** and regenerate the LCu^{I} species.

In summary, a photoinduced, copper-catalyzed three-component radical cross-coupling of *gem*-dialkylthio 1,3-enynes, cycloketone oxime esters, and boronic acids was developed to access highly functionalized aryl-2-thienyl sulfides with good chemo- and diastereoselectivities. The synthetic protocol features simultaneous formation of four new C−C and C−S bonds and construction of a carbocycle and a thiophene ring in one pot. This work provides a direct route to highly functionalized thiophene derivatives.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c01645.

Experimental materials and procedures, NMR of compounds, and X-ray crystallographic analysis for compound **4a** (CCDC 1949838) (PDF)

Accession Codes

CCDC 1949838 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

Zhengkun Yu − *Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, P. R. China; Innovation Academy for Green Manufacture, Chinese Academy of Sciences, Beijing 100190, P. R. China; State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, P. R. China;* orcid.org/0000-0002-9908-0017; Email: zkyu@dicp.ac.cn

Yong-Gui Zhou − *Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, P. R. China;* orcid.org/0000-0002-3321-5521; Email: ygzhou@dicp.ac.cn

Authors

Jiang Lou − *Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, P. R. China; University of Chinese Academy of Sciences, Beijing 100049, P. R. China;* orcid.org/0000-0002-5653-1359

Juan Ma − *Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, P. R. China; University of Chinese Academy of Sciences, Beijing 100049, P. R. China*

Bao-Hua Xu − *Innovation Academy for Green Manufacture, Chinese Academy of Sciences, Beijing 100190, P. R. China;* orcid.org/0000-0002-7222-4383

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.0c01645

https://dx.doi.org/10.1021/acs.orglett.0c01645
Org. Lett. 2020, 22, 5202−5206

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful to the National Natural Science Foundation of China (21672209 and 21871253).

■ REFERENCES

(1) (a) Wang, N.; Saidhareddy, P.; Jiang, X. Construction of Sulfur-Containing Moieties in the Total Synthesis of Natural Products. *Nat. Prod. Rep.* **2020**, *37*, 246−275. (b) Scott, K. A.; Njardarson, J. T. Analysis of US FDA-Approved Drugs Containing Sulfur Atoms. *Top. Curr. Chem. (Z)* **2018**, *376*, 5.

(2) Alcaraz, M.-L.; Atkinson, S.; Cornwall, P.; Foster, A. C.; Gill, D. M.; Humphries, L. A.; Keegan, P. S.; Kemp, R.; Merifield, E.; Nixon, R. A.; Noble, A. J.; O'Beirne, D.; Patel, Z. M.; Perkins, J.; Rowan, P.; Sadler, P.; Singleton, J. T.; Tornos, J.; Watts, A. J.; Woodland, I. A. Efficient Syntheses of AZD4407 *via* Thioether Formation by Nucleophilic Attack of Organometallic Species on Sulphur. *Org. Process Res. Dev.* **2005**, *9*, 555−569.

(3) Tang, H.; Leung, L.; Saturno, G.; Viros, A.; Smith, D.; Di Leva, G.; Morrison, E.; Niculescu-Duvaz, D.; Lopes, F.; Johnson, L.; Dhomen, N.; Springer, C.; Marais, R. Lysyl Oxidase Drives Tumour Progression by Trapping EGF Receptors at the Cell Surface. *Nat. Commun.* **2017**, *8*, 14909.

(4) Hicks, R. G.; Nodwell, M. B. Synthesis and Electronic Structure Investigations of α,ω-Bis(arylthio)oligothiophenes: Toward Understanding Wire-Linker Interactions in Molecular-Scale Electronic Materials. *J. Am. Chem. Soc.* **2000**, *122*, 6746−6753.

(5) (a) Hosseinian, A.; Arshadi, A.; Sarhandi, S.; Monfared, A.; Vessally, E. Direct C−H Bond Sulfenylation of (Het)arenes Using Sulfonyl Hydrazides as Thiol Surrogate: A Review. *J. Sulfur Chem.* **2019**, *40*, 289−311. (b) Li, L.; Ding, Y. Recent Advances in the Synthesis of Thioether. *Mini-Rev. Org. Chem.* **2017**, *14*, 407−431.

(6) (a) Capella, L.; Montevecchi, P. C.; Navacchia, M. L. Radical Sequential Processes Promoted by 1,5-Radical Translocation Reaction: Formation and [3 + 2] Anulation of Alkenesulfanyl Radicals. *J. Org. Chem.* **1996**, *61*, 6783−6789. (b) Gong, X.; Wang, M.; Ye, S.; Wu, J. Synthesis of 3-(Methylsulfonyl)benzo[*b*]thiophenes from Methyl(2-alkynylphenyl)sulfanes and Sodium Metabisulfite *via* a Radical Relay Strategy. *Org. Lett.* **2019**, *21*, 1156−1160. (c) Wan, D.; Yang, Y.; Liu, X.; Li, M.; Zhao, S.; You, J. Radical Cyclization of Arenesulfonyl Chlorides and Alkynes: A Rapid Access to π-Conjugated Benzothiophenes. *Eur. J. Org. Chem.* **2016**, *2016*, 55−59. (d) Zhang, G.; Yi, H.; Chen, H.; Bian, C.; Liu, C.; Lei, A. Trisulfur Radical Anion as the Key Intermediate for the Synthesis of Thiophene *via* the Interaction between Elemental Sulfur and NaO^{t}Bu. *Org. Lett.* **2014**, *16*, 6156−6159. (e) Agrawal, A. R.; Kumar, N. R.; Debnath, S.; Das, S.; Kumar, C.; Zade, S. S. Radical-Cascade Avenue for 3,4-Fused-Ring-Substituted Thiophenes. *Org. Lett.* **2018**, *20*, 4728−4731.

(7) (a) He, Y.; Lou, J.; Wu, P.; Zhou, Y.-G.; Yu, Z. K. Copper-Catalyzed Annulative Coupling of *S*,*S*-Disubstituted Enones with Diazo Compounds to Access Highly Functionalized Thiophene Derivatives. *J. Org. Chem.* **2020**, *85*, 1044−1053. (b) Garg, P.; Singh, A. Unmasking Dipole Character of Acyl Ketene Dithioacetals *via* a Cascade Reaction with Arynes: Synthesis of Benzo[*b*]thiophenes. *Org. Lett.* **2018**, *20*, 1320−1323. (c) Fang, G.; Li, J.; Wang, Y.; Gou, M.; Liu, Q.; Li, X.; Bi, X. An Atom-Economic Route to Thiophenes and 2,2′-Bithiophenes by Intramolecular Transannulation of *gem*-Dialkylthio Enynes. *Org. Lett.* **2013**, *15*, 4126−4129.

(8) (a) Yi, H.; Zhang, G.; Wang, H.; Huang, Z.; Wang, J.; Singh, A. K.; Lei, A. Recent Advances in Radical C−H Activation/Radical Cross-Coupling. *Chem. Rev.* **2017**, *117*, 9016−9085. (b) Xie, J.; Jin, H.; Hashmi, A. S. K. The Recent Achievements of Redox-Neutral Radical C−C Cross-Coupling Enabled by Visible-Light. *Chem. Soc. Rev.* **2017**, *46*, 5193−5203. (c) Studer, A.; Curran, D. P. Catalysis of Radical Reactions: A Radical Chemistry Perspective. *Angew. Chem., Int. Ed.* **2016**, *55*, 58−102.

(9) (a) Yu, X.-H.; Zhao, Q.-Q.; Chem, J.; Xiao, W.-J.; Chen, J.-R. When Light Meets Nitrogen-Centered Radicals: From Reagents to Catalysts. *Acc. Chem. Res.* **2020**, *53*, 1066−1083. (b) Zard, S. Z. Recent Progress in the Generation and Use of Nitrogen-Centred Radicals. *Chem. Soc. Rev.* **2008**, *37*, 1603−1618.

(10) (a) Li, Z.; Torres-Ochoa, R. O.; Wang, Q.; Zhu, J. Functionalization of Remote C(sp^3)−H Bonds Enabled by Copper-Catalyzed Coupling of *O*-acyloximes with Terminal Alkynes. *Nat. Commun.* **2020**, *11*, 403. (b) Zhao, B.; Wu, Y.; Yuan, Y.; Shi, Z. Copper-Catalysed Csp^3−Csp Cross-Couplings Between Cyclobutanone Oxime Esters and Terminal Alkynes Induced by Visible Light. *Chem. Commun.* **2020**, *56*, 4676−4679. (c) Wang, T.; Wang, Y.-N.; Wang, R.; Zhang, B.-C.; Yang, C.; Li, Y.-L.; Wang, X.-S. Enantioselective Cyanation via Radical-Mediated C−C Single Bond Cleavage for Synthesis of Chiral Dinitriles. *Nat. Commun.* **2019**, *10*, 5373. (d) Chen, J.; Wang, P.-Z.; Lu, B.; Liang, D.; Yu, X.-H.; Xiao, W.-J.; Chen, J.-R. Enantioselective Radical Ring-Opening Cyanation of Oxime Esters by Dual Photoredox and Copper Catalysis. *Org. Lett.* **2019**, *21*, 9763−9768. (e) Lu, B.; Cheng, Y.; Chen, L.-Y.; Chen, J.-R.; Xiao, W.-J. Photoinduced Copper-Catalyzed Radical Aminocarbonylation of Cycloketone Oxime Esters. *ACS Catal.* **2019**, *9*, 8159−8164. (f) Dauncey, E. M.; Dighe, S. U.; Douglas, J. J.; Leonori, D. A Dual Photoredox-Nickel Strategy for Remote Functionalization *via* Iminyl Radicals: Radical Ring-Opening-Arylation, -Vinylation and -Alkylation Cascades. *Chem. Sci.* **2019**, *10*, 7728−7733. (g) Zhang, J.-J.; Duan, X.-H.; Wu, Y.; Yang, J.-C.; Guo, L.-N. Transition-Metal Free C−C Bond Cleavage/Borylation of Cycloketone Oxime Esters. *Chem. Sci.* **2019**, *10*, 161−166. (h) Dauncey, E. M.; Morcillo, S. P.; Douglas, J. J.; Sheikh, N. S.; Leonori, D. Photoinduced Remote Functionalisations by Iminyl Radical Promoted C−C and C−H Bond Cleavage Cascades. *Angew. Chem., Int. Ed.* **2018**, *57*, 744−748. (i) Yu, X.-Y.; Chen, J.-R.; Wang, P.-Z.; Yang, M.-N.; Liang, D.; Xiao, W.-J. 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.

(11) (a) Yu, X.-Y.; Zhao, Q.-Q.; Chen, J.; Chen, J.-R.; Xiao, W.-J. Copper-Catalyzed Radical Cross-Coupling of Redox-Active Oxime Esters, Styrenes, and Boronic Acids. *Angew. Chem., Int. Ed.* **2018**, *57*, 15505−15509. (b) Chen, J.; He, B.-Q.; Wang, P.-Z.; Yu, X.-Y.; Zhao, Q.-Q.; Chen, J.-R.; Xiao, W.-J. Photoinduced, Copper-Catalyzed Radical Cross-Coupling of Cycloketone Oxime Esters, Alkenes, and Terminal Alkynes. *Org. Lett.* **2019**, *21*, 4359−4364.

(12) (a) Gu, Q.-S.; Li, Z.-L.; Liu, X.-Y. Copper(I)-Catalyzed Asymmetric Reactions Involving Radicals. *Acc. Chem. Res.* **2020**, *53*, 170−181. (b) Kaiser, D.; Klose, I.; Oost, R.; Neuhaus, J.; Maulide, N. Bond-Forming and -Breaking Reactions at Sulfur(IV): Sulfoxides, Sulfonium Salts, Sulfur Ylides, and Sulfinate Salts. *Chem. Rev.* **2019**, *119*, 8701−8780. (c) Wang, F.; Chen, P.; Liu, G. Copper-Catalyzed Radical Relay for Asymmetric Radical Transformations. *Acc. Chem. Res.* **2018**, *51*, 2036−2046.

(13) (a) Wang, Q. N.; Liu, Z. Q.; Lou, J.; Yu, Z. K. Palladium-Catalyzed C−S Bond Cleavage with Allenoates: Synthesis of Tetrasubstituted 2-Alkenylfuran Derivatives. *Org. Lett.* **2018**, *20*, 6007−6011. (b) Lou, J.; Wang, Q. N.; Wu, K. K.; Wu, P.; Yu, Z. K. Iron-Catalyzed Oxidative C−H Functionalization of Internal Olefins for the Synthesis of Tetrasubstituted Furans. *Org. Lett.* **2017**, *19*, 3287−3290.

(14) Ming, W.; Liu, X.; Wang, L.; Liu, J.; Wang, M. Tandem Thien- and Benzannulations of α-Alkenoyl-α-alkynyl Ketene Dithioacetals with Cyanoacetates: Synthesis of Functionalized Benzo[*b*]thiophenes. *Org. Lett.* **2015**, *17*, 1746−1749.

(15) (a) Tang, S.; Liu, Y.; Gao, X.; Wang, P.; Huang, P.; Lei, A. Multi-Metal-Catalyzed Oxidative Radical Alkynylation with Terminal Alkynes: A New Strategy for C(sp^3)−C(sp) Bond Formation. *J. Am. Chem. Soc.* **2018**, *140*, 6006−6013. (b) Lu, Q.; Zhang, J.; Peng, P.; Zhang, G.; Huang, Z.; Yi, H.; Miller, J. T.; Lei, A. Operando X-ray Absorption and EPR Evidence for a Single Electron Redox Process in Copper Catalysis. *Chem. Sci.* **2015**, *6*, 4851−4854.

https://dx.doi.org/10.1021/acs.orglett.0c01645
Org. Lett. 2020, 22, 5202−5206