Organic Letters

Letter

Cite This: *Org. Lett.* XXXX, XXX, XXX−XXX

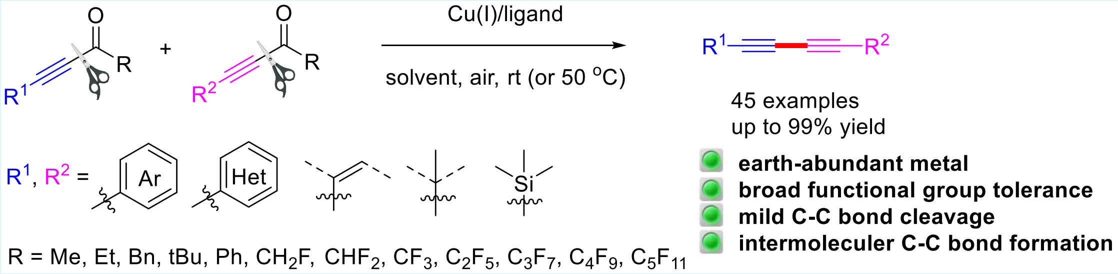
pubs.acs.org/OrgLett

Copper-Mediated Deacylative Coupling of Ynones via C−C Bond Activation under Mild Conditions

Lili Feng, Tingjun Hu, Saisai Zhang, Heng-Ying Xiong,* and Guangwu Zhang*

Institute of Organic Functional Molecules, Engineering Laboratory of Fire Retardant and Functional Materials, College of Chemistry and Chemical Engineering, Henan University, Kaifeng 475004, P.R. China

Supporting Information

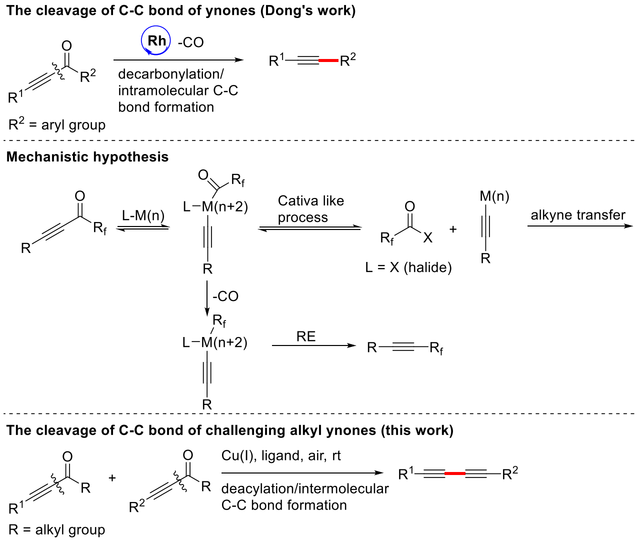


ABSTRACT: The intermolecular deacylative coupling of unstrained ynones via C−C bond activation was accomplished by a CuCl−bpy system under mild reaction conditions. This protocol features facile cleavage of the C−C bond at room temperature, broad substrate scope, and efficient construction of important symmetric and unsymmetrical 1,3-diyne adducts through homo or cross coupling of ynones, respectively. The preliminary mechanistic investigations indicated that an acyl copper(III) complex is likely involved in this process.

The inert bonds such as a carbon−hydrogen (C−H), carbon−oxygen (C−O), carbon−nitrogen (C−N), and carbon−carbon (C−C) bonds are prevailed linkages in organic molecules. Consequently, the transition-metal-promoted activation of these unactivated bonds in easily accessible feedstocks has led to a variety of novel C−C bond formations, benefiting a broad scope of communities such as medicinal chemistry, agricultural, and material chemistry.[1] Although the C−C bond activation has been comparatively underdeveloped,[2] the highly selective functionalization of ketones, through a decarbonylation process, has gained considerable attention since Teranishi and co-workers' pioneering work on Rh-mediated decarbonylation of diketone reported in 1974.[3] Thanks to the elegant seminal works of Murakami/Ito,[4] Jun,[5] Douglas,[6] Shi,[7] Dong,[8] and Wang,[9] which either use stained ring systems or introduce chelation groups to render C−C bond cleavage, some specific ketones have emerged as suitable precursors for C−C bond activation. On the other hand, the contributions from Chatani,[10] Dong,[11] Lei,[12] Jiao,[13] and Li[14] represented a milestone on functionalization of C−C bonds of more challenging less strained or unstrained ketones. Despite these advances, there are several limitations remaining on C−C bond activation of these substrates: (1) the use of noble metals in some transformations and (2) the frequent employment of severe reaction conditions.

Inspired by the decarbonylation transformations of ynones from the Dong group in which aryl ketones were compatible while alkyl ketones were not well tolerated in most cases (Scheme 1, top),[11c] we wondered whether the installation of a fluorinated alkyl as an electron-withdrawing group onto the ynone structure could tune the reactivity, hence realizing mild C−C bond cleavage and/or even altering the reaction pathway since the carbon−alkyne bonds of the fluorinated moieties are more polarized compared to the nonfluorinated ones.

Scheme 1. Approaches for the C−C Bond Activation of Ynones



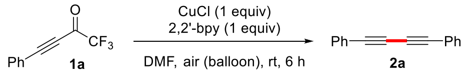
Received: October 18, 2019

DOI: 10.1021/acs.orglett.9b03684
Org. Lett. XXXX, XXX, XXX−XXX

However, the key scientific concern in this conception is an unprecedented insertion of a metal complex into the bond between the alkynyl and fluorinated carbonyl groups. Besides the known oxidative addition of Rh(I) into a nonfluorinated acyl−alkyne bond, Sanford and co-workers have revealed the mild oxidative addition of a fluorinated carbonyl compound to a low valent transition metal complex.[15] Accordingly, it is rational to speculate the feasibility of the oxidative addition step. If it occurs, the putative fluorinated acyl metal complex could either undergo regularly subsequent extrusion of CO and reductive elimination to give a fluorinated alkyl substituted internal alkyne or proceed through a reductive elimination, like a "Cativa process",[16] to afford a fluorinated acetyl halide and an alkynyl-metal species (Scheme 1, middle). The latter could account for various alkynyl transfer reactions. In this regard, considering that the fluorinated acyl metal species were reluctant to decarbonylate unless upon the treatment of harsh reaction conditions,[15] the deacylative alkynyl transfer route should be preferred under regular or even milder conditions. In this report, we disclose a Cu-promoted mild deacylation of challenging alkyl ynones to access important 1,3-diyne adducts (Scheme 1, bottom), a core skeleton existing in a wide range of natural products and materials.[17]

We initiated our hypothesis by employing phenylethynyl trifluoromethyl ketone as the model substrate in the presence of a variety of Rh precatalysts that have proved useful in the C−C bond cleavage process. Unfortunately, all the attempts led to either the decomposition of the starting material or an undefined reaction mixture, confirming the incompatibility of the alkyl ynones with the Rh system that was formerly reported.[11c] In view of the recent interest in copper-promoted C−C bond activation, we then switched our attention to the copper system. After intensive endeavors on the exploration of various reaction parameters, we determined that the deacylative coupling of trifluoromethyl ynone could be achieved in the presence of stoichiometric CuCl and the 2,2′-bpy ligand at room temperature, leading to the 1,3-diyne **2a** in 90% yield (Table 1, entry 1). The employment of a catalytic amount of ligand or CuCl resulted in a decreased or poor yield (entries 2 and 3). Other copper(I) salts showed medium to good reactivities, providing the coupling product in 55−78% yield (entries 4−6), while copper(II) salts were totally inefficient upon testing (entries 7−9). These results indicate that a low valent copper is essential for the oxidative addition step. Furthermore, other ligands including pyridine, substituted 2,2′-bpy, and 1,10-phen were less efficient compared to 2,2′-bpy (entries 10−13). It is worth mentioning that no desired product was detected when utilizing a phosphine ligand. The replacement of DMF with other polar solvents such as THF, CH_3CN, or DMSO all led to the erosion of yields (entries 14−16). The N_2 or O_2 atmosphere had a deleterious effect on reaction outcomes (entries 17−18), revealing that the amount of O_2 is crucial for this reaction. Elevated temperature did not further improve the efficiency (entry 19). Finally, when the reaction was set to 0 °C, the C−C bond cleavage also smoothly occurred albeit in slightly lower yield (entry 20).

Table 1. Impact of Reaction Parameters on Deacylative Coupling of Trifluoromethyl Ynone[a]



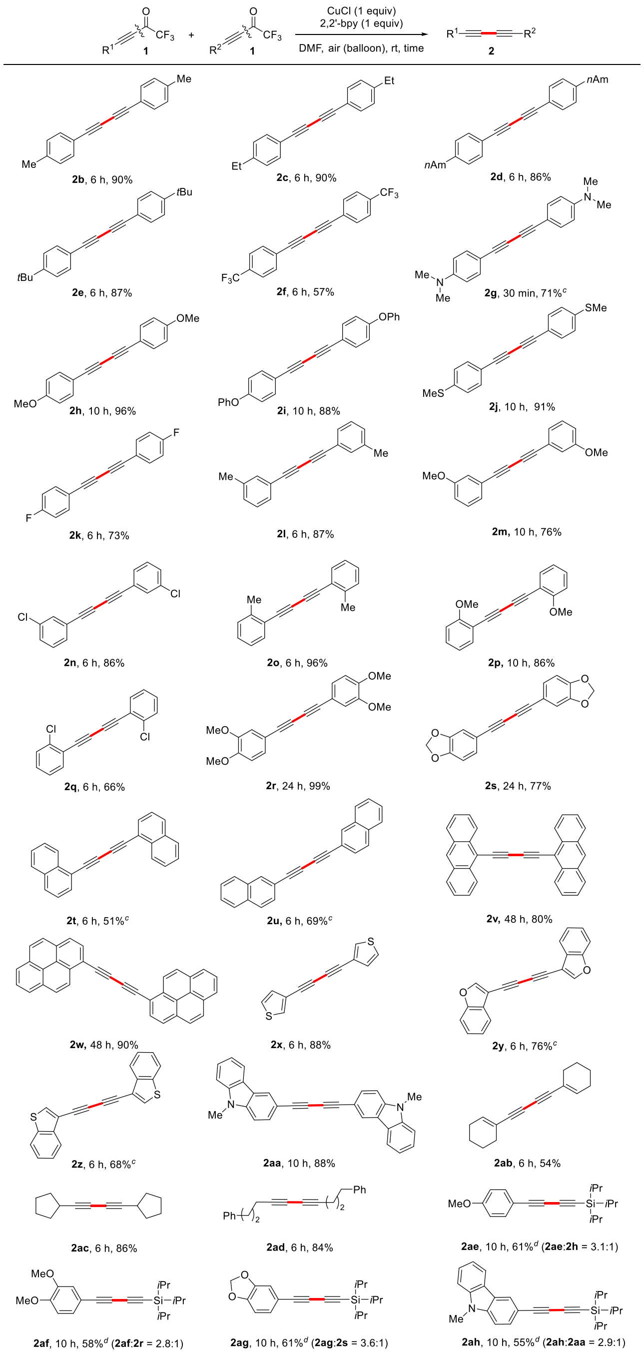
entry	change from the standard conditions	yield (%)[b]
1	none	90
2	2,2′-bpy (50%)	63
3	CuCl (50%)	13
4	CuBr instead of CuCl	78
5	CuI instead of CuCl	70
6	$Cu(MeCN)_4PF_6$ instead of CuCl	55
7	$CuCl_2$ instead of CuCl	12
8	CuF_2 instead of CuCl	-
9	$Cu(OAc)_2$ instead of CuCl	15
10	pyridine instead of 2,2′-bpy	70
11	bis(MeO)-bpy instead of 2,2′-bpy	70
12	2,2′-bipyrimidine instead of 2,2′-bpy	20
13	1,10-phen instead of 2,2′-bpy	73
14	THF instead of DMF	63
15	CH_3CN instead of DMF	77
16	DMSO instead of DMF	46
17	in N_2 (balloon)	57
18	in O_2 (balloon)	77
19	at 50 °C	90
20	at 0 °C	78

[a]Ynone **1a** (0.3 mmol, 1 equiv), CuCl (0.3 mmol, 1 equiv), and 2,2′-bpy (0.3 mmol, 1 equiv) in DMF (2 mL) under an air balloon at room temperature for 6 h. [b]Isolated yield.

With the optimal reaction conditions in hand, we next probed the scope of the alkyne moiety. As depicted in Scheme 2, the arenes with various substitution patterns were well tolerated, affording the homo-coupling products in modest to excellent yields (**2b**−**2aa**, Scheme 2). A series of functional groups including amine, ether, thioether, and oxygen-, nitrogen-, and sulfur-containing hetero cycles were compatible with the reaction conditions (**2g**−**j**, **2m**, **2p**, and **2r**−**s**). Moreover, halogens (F and Cl) were also applicable, showcasing the potential for post functionalization of the products (**2k**, **2n**, and **2q**). Remarkablely, diynes bearing polyaromatics including naphthalene, benzofuran, benzothiophene, anthracene, pyrene, and carbazole, which may have multiple utilizations in material chemistry, have been successfully assembled with the current approach (**2t**−**w**, **2y**−**aa**). In addition, alkenyl- and alkyl-substituted alkynes were also proved to be suitable substrates, furnishing the corresponding diyne products in moderate to good yield (**2ab**−**ad**). Furthermore, the current methodology was not limited to homo coupling, and cross coupling between two different alkynes also underwent C−C bond cleavage/C−C bond formation, producing the unsymmetrical coupling products as the major products in good yields (**2ae**−**ah**).

In terms of substitution on the ketone part, the scope of this method is also broad as shown in Scheme 3. Alkyl groups including fluorinated and nonfluorinated linear chains smoothly undertook the C−C bond activation/homo-coupling process to give a phenyl diyne in moderate to excellent yield (**1af**−**an**). It was also noticed that there is an apparent "fluoro-substitution effect" on reaction outcomes, in which increasing the numbers of fluoride atoms imparted a positive impact on reaction efficiency. Such a tendency was consistent with our original hypothesis that, due to the more polarized carbon−alkyne bond of the fluorinated ynones compared to non- or less fluorinated ones, the reactivities are enhanced. Interestingly, when the number of a F atom reached 11 (**1al**), slightly decreased coupling yield was observed. In addition, the substitution on ketone with a strong steric hindrance group

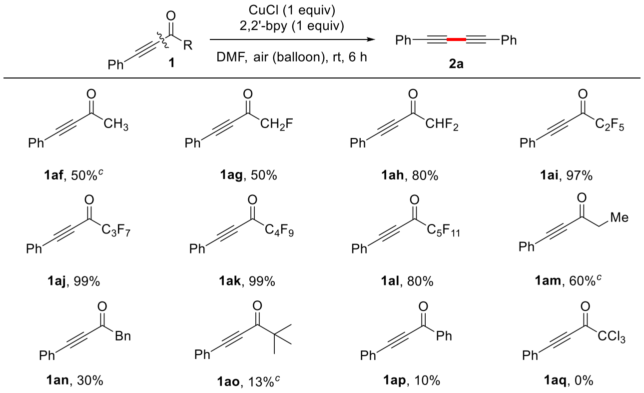
Scheme 2. Scope of the Alkyne Moiety[a,b]



[a] Ynone **1** (0.3 mmol, 1 equiv), CuCl (0.3 mmol, 1 equiv), and 2,2′-bpy (0.3 mmol, 1 equiv) in DMF (2 mL) under an air balloon at room temperature. [b] Isolated yield. [c] At 50 °C. [d] Cross-coupling reaction conditions are ynone **1** (0.1 mmol, 1 equiv), ynone **1ae** (0.15 mmol, 1.5 equiv), CuCl (0.2 mmol, 2 equiv), and 2,2′-bpy (0.2 mmol, 2 equiv) in DMF (2 mL) under an air balloon at room temperature for 10 h.

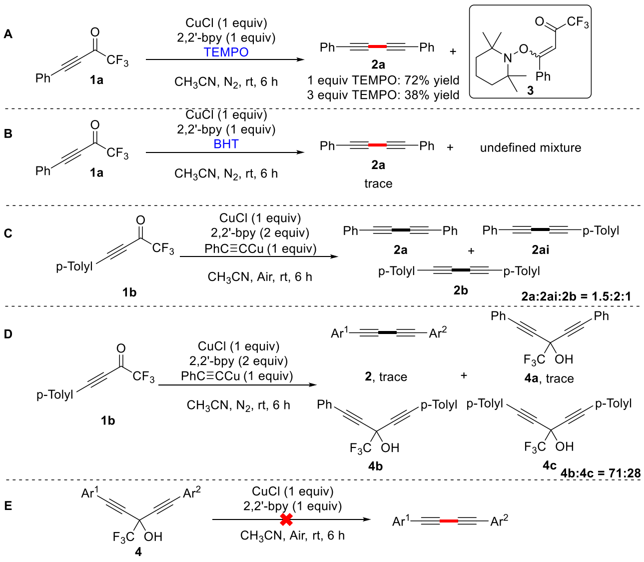
such as *t*Bu hampered the coupling process, with only 13% yield obtained (**1ao**). It is notable that C−C bond activation of phenyl ynone also occurred, albeit in a poor yield (**1ap**). When a CCl$_3$ group was introduced onto the ynone structure as an electron-withdrawing group, fast decomposition of this substrate was observed with no coupling product detected (**1aq**).

Scheme 3. Scope of the Ketone Moiety[a,b]



[a] Ynone **1** (0.3 mmol, 1 equiv), CuCl (0.3 mmol, 1 equiv), and 2,2′-bpy (0.3 mmol, 1 equiv) in DMF (2 mL) under an air balloon at room temperature for 6 h. [b] Isolated yield. [c] At 50 °C.

Scheme 4. Investigation of Reaction Mechanism

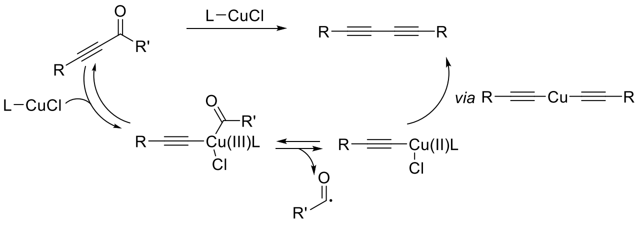


To probe the reaction mechanism, several preliminary investigations were conducted. The addition of the radical scavenger TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) led to decreased yield of diyne, along with the isolated 1,1,1-trifluoro-4-phenyl-4-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)-but-3-en-2-one (**3**) (Scheme 4A). Interestingly, the introduction of BHT (2,6-di-*tert*-butyl-*p*-cresol) into a reaction mixture totally prohibited the formation of diyne, leading to an undefined mixture (Scheme 4B). Next, when **1b** was treated with stoichiometric copper phenylacetylide (1 equiv) under standard reaction conditions (in CH$_3$CN, under air), a mixture of homo- and cross-coupling products were formed (ratio: **2a**:**2ai**:**2b** = 1.5:2:1) (Scheme 4C). When this reaction was carried out under N$_2$, 1,2-addition products of copper acetylide with ynones **4** were observed (ratio: **4b**:**4c** = 71:28) with a trace amount of diyne product (Scheme 4D). These results implied that alkynyl-Cu(I) species might not be the real intermediate. It is worth mentioning that the formation of **4c** indicated a copper(II) *p*-tolylacetylide is likely generated during the process. Upon the treatment of the resulting propargyl alcohols with standard conditions (in CH$_3$CN, under air), the starting materials were intact (Scheme 4E), implying that 1,2-addition adducts were not the intermediates leading to the diyne products.

An electrospray ionization mass spectrometry (ESI-MS) method was also performed to gain insight into the reaction mechanism. It was shown that an ESI-MS measurement of a reaction mixture of **1a** under standard conditions presented a base peak at *m/z* 264.7 at 5 min of reaction time, related to the existence of the copper-alkyl species [Cu(phenyl ethynyl)$_2$], which was slowly consumed and finally disappeared within 2 h (see SI).

Based on the above observations and previous reports,[2l,11a,b,18,19] we proposed a plausible reaction mechanism (Scheme 5). First, the oxidative addition of the Cu(I) complex onto the acyl−alkyne bond forms the Cu(III) intermediate, which then releases a acetyl radical to give Cu(II)-alkynyl species. The latter then follows the Glaser process to give 1,3-diynes,[20] during which the detected [Cu(phenyl ethynyl)$_2$] might be an important intermediate, leading to the final product.

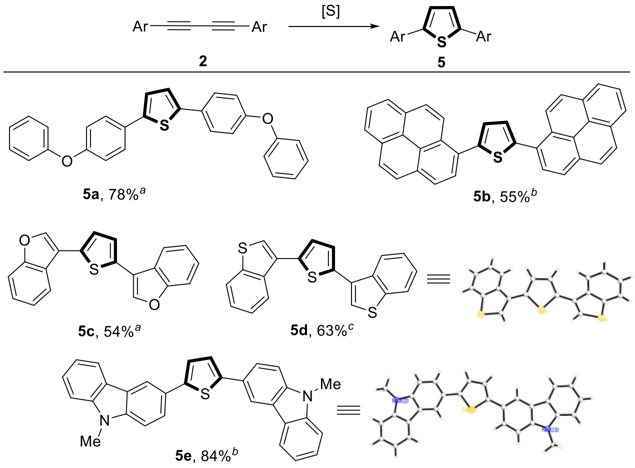
Scheme 5. Proposed Reaction Mechanism



In light of the tremendous application of functionalized thiophenes in materials science such as OPVs, DSSCs, OLEDs, and OFETs,[21] the selected coupling products 1,3-diynes were cyclized with a sulfur source by following slightly modified procedures[22] to afford thiophene-bridged polycycles in moderate to good yields (Scheme 6). It is worth noting that most of these thiophene derivatives are unprecedented structures, and structures of **5d** and **5e** were definitely determined by X-ray diffraction. An initial investigation of optical properties of these products was conducted. The UV spectra of **5a−e** show absorption maximum bands at 275−372 nm in CH_2Cl_2, which correspond to the $\pi-\pi^*$ transition of arenes and thiophene. Emission maxima were observed at 411−481 nm in the fluorescence spectra of **5a−e** in CH_2Cl_2. As can be seen from the figures in the SI, the order of fluorescence intensity of molecules is **5e** > **5a** > **5b** > **5d** > **5c**, which is related to the conjugation degree of p electrons. It is noticed that **5e** exhibits an intense blue luminescence peak at around 416 nm and can be utilized as a blue emitter for electroluminescence (EL) devices.

In conclusion, we have described the first copper-mediated deacylative coupling of ynones via C−C bond activation under mild reaction conditions. This approach demonstrates good functional group compatibility and broad substrate scope and is applicable for both homo and cross coupling of ynones, delivering a range of substituted 1,3-diynes from moderate to excellent yields. This method could be a complementary strategy to the traditional Glaser route for the synthesis of 1,3-diynes. In addition, the detection of the alkynyl-copper species by ESI-MS indicates the potential of other alkyne transfer reactions through the deacylation of ynones. Furthermore, the cyclization of selected 1,3-diynes with a sulfur source furnished 2,5-disubstituted thiophenes, which are of great interest for material purposes. The further systematic investigation of the reaction mechanism as well as merging the C−C bond activation of ynones with other transformations are underway in our laboratory.

Scheme 6. Derivation of the Selected Coupling Adducts



[a]Reaction conditions: diyne (1 equiv), sulfur powder (3 equiv), and NaHS (6 equiv) in 2.0 mL of DMF at rt under N_2 for 5 h. [b]Reaction conditions: diyne (0.1 mmol, 1 equiv), sulfur powder (3 equiv), and NaHS (6 equiv) in 2.0 mL of DMSO at 80 °C under N_2 for 12 h. [c]Reaction conditions: diyne (0.1 mmol, 1 equiv), sulfur powder (0.3 mmol, 3 equiv), and NaOtBu (0.6 mmol, 6 equiv) in 2.0 mL of DMF/HO*t*Bu (v:v = 3:1) at rt under N_2 for 5 h.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.9b03684.

> General information; Materials; General procedure for the synthesis of derivatives **1**; Purification and characterization of derivatives **1**; General procedure for the synthesis of derivatives **2a−2ad**; General procedure for the synthesis of derivatives **2ae−2ah**; Purification and characterization of derivatives **2**; Investigation of reaction mechanism; Procedure for the synthesis of **5a** and **5c**; Procedure for the synthesis of **5b** and **5e**; Procedure for the synthesis of **5d**; Purification and characterization of derivatives **5**; Procedure for the ESI-MS study of the reaction mixture; Absorption spectra (UV) and fluorescence spectra of **5a−e** in CH_2Cl_2; References; NMR spectra of derivatives **1**; NMR spectra of derivatives **2**; NMR spectra of derivatives **3**; NMR spectra of control experiments; and NMR spectra of derivatives **5** (PDF)

Accession Codes

CCDC 1918953 and 1919696 contain 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

*E-mail: gw.zhangchem@hotmail.com
*E-mail: xionghengying@vip.henu.edu.cn

ORCID

Guangwu Zhang: 0000-0001-8365-4197

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research was supported by Henan University, the National Natural Science Foundation of China (21801061). Professor Pengtao Ma (HNU) is thanked for the X-ray structure. Professor Xunyong Liu (LDU) is thanked for the helpful discussion on optical studies.

■ REFERENCES

(1) *Activation of Unreactive Bonds and Organic Synthesis; Top. Organomet. Chem.* 3; Murai, S., Ed.; Springer-Verlag: Berlin, 1999.

(2) (a) Jun, C. H. Transition metal-catalyzed carbon–carbon bond activation. *Chem. Soc. Rev.* **2004**, *33*, 610–618. (b) Satoh, T.; Miura, M. Catalytic Processes Involving *β*-Carbon Elimination. *Top. Organomet. Chem.* **2005**, *14*, 1–20. (c) Jun, C. H.; Park, J. W. Directed C – C Bond Activation by Transition Metal Complexes. *Top. Organomet. Chem.* **2007**, *24*, 117–143. (d) Necas, D.; Kotora, M. Rhodium-Catalyzed C-C Bond Cleavage Reactions. *Curr. Org. Chem.* **2007**, *11*, 1566–1591. (e) Korotvicka, A.; Necas, D.; Kotora, M. Rhodium-catalyzed C-C Bond Cleavage Reactions - An Update. *Curr. Org. Chem.* **2012**, *16*, 1170–1214. (f) Seiser, T.; Saget, T.; Tran, D. N.; Cramer, N. Cyclobutanes in catalysis. *Angew. Chem., Int. Ed.* **2011**, *50*, 7740–7752. (g) Jiao, L.; Yu, Z.-X. Vinylcyclopropane Derivatives in Transition-Metal-Catalyzed Cycloadditions for the Synthesis of Carbocyclic Compounds. *J. Org. Chem.* **2013**, *78*, 6842–6848. (h) Dermenci, A.; Coe, J. W.; Dong, G. Direct activation of relatively unstrained carbon–carbon bonds in homogeneous systems. *Org. Chem. Front.* **2014**, *1*, 567–581. (i) Dermenci, A.; Dong, G. Decarbonylative C-C bond forming reactions mediated by transition metals. *Sci. China: Chem.* **2013**, *56*, 685–701. (j) Chen, F.; Wang, T.; Jiao, N. Recent advances in transition-metal-catalyzed functionalization of unstrained carbon-carbon bonds. *Chem. Rev.* **2014**, *114*, 8613–8661. (k) *C–C Bond Activation; Topics in Current Chemistry*; Dong, G., Ed.; Springer: Berlin, 2014; Vol. *346*. (l) Souillart, L.; Cramer, N. Catalytic C–C Bond Activations via Oxidative Addition to Transition Metals. *Chem. Rev.* **2015**, *115*, 9410–9464. (m) Murakami, M.; Ishida, N. Potential of Metal-Catalyzed C–C Single Bond Cleavage for Organic Synthesis. *J. Am. Chem. Soc.* **2016**, *138*, 13759–13769. (n) Song, F.; Gou, T.; Wang, B.-Q.; Shi, Z.-J. Catalytic activations of unstrained C–C bond involving organometallic intermediates. *Chem. Soc. Rev.* **2018**, *47*, 7078–7115.

(3) Kaneda, K.; Azuma, H.; Wayaku, M.; Tehanishi, S. Decarbonylation of *α*-and *β*-Diketones Catalyzed by Rhodium Compounds. *Chem. Lett.* **1974**, *3*, 215–216.

(4) (a) Murakami, M.; Itahashi, T.; Ito, Y. Catalyzed Intramolecular Olefin Insertion into a Carbon–Carbon Single Bond. *J. Am. Chem. Soc.* **2002**, *124*, 13976–13977. (b) Murakami, M.; Ashida, S.; Matsuda, T. Nickel-Catalyzed Intermolecular Alkyne Insertion into Cyclobutanones. *J. Am. Chem. Soc.* **2005**, *127*, 6932–6933.

(5) (a) Suggs, J. W.; Jun, C.-H. Directed cleavage of carbon-carbon bonds by transition metals: the *α*-bonds of ketones. *J. Am. Chem. Soc.* **1984**, *106*, 3054–3056. (b) Suggs, J. W.; Jun, C.-H. Synthesis of a chiral rhodium alkyl via metal insertion into an unstrained C-C bond and use of the rate of racemization at carbon to obtain rhodium-carbon bond dissociation energy. *J. Am. Chem. Soc.* **1986**, *108*, 4679–4681.

(6) (a) Dreis, A. M.; Douglas, C. J. Catalytic Carbon–Carbon *σ* Bond Activation: An Intramolecular Carbo-Acylation Reaction with Acylquinolines. *J. Am. Chem. Soc.* **2009**, *131*, 412–413. (b) Wentzel, M. T.; Reddy, V. J.; Hyster, T. K.; Douglas, C. J. Chemoselectivity in catalytic C-C and C-H bond activation: controlling intermolecular carboacylation and hydroarylation of alkenes. *Angew. Chem., Int. Ed.* **2009**, *48*, 6121–6123.

(7) Lei, Z.; Li, H.; Li, Y.; Zhang, X.; Chen, K.; Wang, X.; Sun, J.; Shi, Z.-J. Extrusion of CO from aryl ketones: rhodium(I)-catalyzed C-C bond cleavage directed by a pyridine group. *Angew. Chem., Int. Ed.* **2012**, *51*, 2690–2694.

(8) (a) Xu, T.; Savage, N. A.; Dong, G. Rhodium(I)-Catalyzed Decarbonylative Spirocyclization through C-C Bond Cleavage of Benzocyclobutenones: An Efficient Approach to Functionalized Spirocycles. *Angew. Chem., Int. Ed.* **2014**, *53*, 1891–1895. (b) Xu, T.; Dong, G. Coupling of sterically hindered trisubstituted olefins and benzocyclobutenones by C-C activation: total synthesis and structural revision of cycloinumakiol. *Angew. Chem., Int. Ed.* **2014**, *53*, 10733–10736. (c) Zeng, R.; Dong, G. Rh-Catalyzed Decarbonylative Coupling with Alkynes via C–C Activation of Isatins. *J. Am. Chem. Soc.* **2015**, *137*, 1408–1411. (d) Zhou, X.; Dong, G. (4 + 1) vs (4 + 2): Catalytic Intramolecular Coupling between Cyclobutanones and Trisubstituted Allenes via C–C Activation. *J. Am. Chem. Soc.* **2015**, *137*, 13715–13721. (e) Chen, P.; Xu, T.; Dong, G. Divergent syntheses of fused *β*-naphthol and indene scaffolds by rhodium-catalyzed direct and decarbonylative alkyne-benzocyclobutenone couplings. *Angew. Chem., Int. Ed.* **2014**, *53*, 1674–1678. (f) Lu, G.; Fang, C.; Xu, T.; Dong, G.; Liu, P. Computational Study of Rh-Catalyzed Carboacylation of Olefins: Ligand-Promoted Rhodacycle Isomerization Enables Regioselective C–C Bond Functionalization of Benzocyclobutenones. *J. Am. Chem. Soc.* **2015**, *137*, 8274–8283. (g) Deng, L.; Chen, M.; Dong, G. Concise Synthesis of (−)-Cycloclavine and (−)-5-epi-Cycloclavine via Asymmetric C–C Activation. *J. Am. Chem. Soc.* **2018**, *140*, 9652–9658. (h) Zhou, X.; Ko, H.; Dong, G. Synthesis of Bridged Cyclopentane Derivatives by Catalytic Decarbonylative Cycloaddition of Cyclobutanones and Olefins. *Angew. Chem., Int. Ed.* **2016**, *55*, 13867–13871. (i) Zhou, X.; Dong, G. Nickel-Catalyzed Chemo- and Enantioselective Coupling between Cyclobutanones and Allenes: Rapid Synthesis of [3.2.2] Bicycles. *Angew. Chem., Int. Ed.* **2016**, *55*, 15091–15095. (j) Deng, L.; Jin, L.; Dong, G. Fused-Ring Formation by an Intramolecular "Cut-and-Sew" Reaction between Cyclobutanones and Alkynes. *Angew. Chem., Int. Ed.* **2018**, *57*, 2702–2706. (k) Deng, L.; Xu, T.; Li, H.; Dong, G. Enantioselective Rh-Catalyzed Carboacylation of C = N Bonds via C–C Activation of Benzocyclobutenones. *J. Am. Chem. Soc.* **2016**, *138*, 369–374. (l) Ko, H. M.; Dong, G. Cooperative activation of cyclobutanones and olefins leads to bridged ring systems by a catalytic [4 + 2] coupling. *Nat. Chem.* **2014**, *6*, 739–744. (m) Sun, T.; Zhang, Y.; Qiu, B.; Wang, Y.; Qin, Y.; Dong, G.; Xu, T. Rhodium(I)-Catalyzed Carboacylation/Aromatization Cascade Initiated by Regioselective C-C Activation of Benzocyclobutenones. *Angew. Chem., Int. Ed.* **2018**, *57*, 2859–2863.

(9) Wang, J.; Chen, W.; Zuo, S.; Liu, L.; Zhang, X.; Wang, J. Direct exchange of a ketone methyl or aryl group to another aryl group through C-C bond activation assisted by rhodium chelation. *Angew. Chem., Int. Ed.* **2012**, *51*, 12334–12338.

(10) Morioka, T.; Nishizawa, A.; Furukawa, T.; Tobisu, M.; Chatani, N. Nickel-Mediated Decarbonylation of Simple Unstrained Ketones through the Cleavage of Carbon–Carbon Bonds. *J. Am. Chem. Soc.* **2017**, *139*, 1416–1419.

(11) (a) Whittaker, R.; Dong, G. Controlled Rh-Catalyzed Mono- and Double-decarbonylation of Alkynyl *α*-Diones To Form Conjugated Ynones and Disubstituted Alkynes. *Org. Lett.* **2015**, *17*, 5504–5507. (b) Dermenci, A.; Whittaker, R. E.; Dong, G. Rh(I)-Catalyzed Decarbonylation of Diynones via C–C Activation: Orthogonal Synthesis of Conjugated Diynes. *Org. Lett.* **2013**, *15*, 2242–2245. (c) Dermenci, A.; Whittaker, R. E.; Gao, Y.; Cruz, F. A.; Yu, Z.-X.; Dong, G. Rh-catalyzed decarbonylation of conjugated ynones via carbon–alkyne bond activation: reaction scope and

mechanistic exploration via DFT calculations. *Chem. Sci.* **2015**, *6*, 3201−3210. (d) Xia, Y.; Lu, G.; Liu, P.; Dong, G. Catalytic activation of carbon-carbon bonds in cyclopentanones. *Nature* **2016**, *539*, 546−550. (e) Xia, Y.; Wang, J.; Dong, G. Distal-Bond-Selective C-C Activation of Ring-Fused Cyclopentanones: An Efficient Access to Spiroindanones. *Angew. Chem., Int. Ed.* **2017**, *56*, 2376−2380. (f) Rong, Z.-Q.; Lim, H. N.; Dong, G. Intramolecular Acetyl Transfer to Olefins by Catalytic C-C Bond Activation of Unstrained Ketones. *Angew. Chem., Int. Ed.* **2018**, *57*, 475−479. (g) Xia, Y.; Wang, J.; Dong, G. Suzuki−Miyaura Coupling of Simple Ketones via Activation of Unstrained Carbon−Carbon Bonds. *J. Am. Chem. Soc.* **2018**, *140*, 5347−5351. (h) Xu, Y.; Qi, X.; Zheng, P.; Berti, C. C.; Liu, P.; Dong, G. Deacylative transformations of ketones via aromatization-promoted C−C bond activation. *Nature* **2019**, *567*, 373−378.

(12) He, C.; Guo, S.; Huang, L.; Lei, A. Copper Catalyzed Arylation/C−C Bond Activation: An Approach toward α-Aryl Ketones. *J. Am. Chem. Soc.* **2010**, *132*, 8273−8275.

(13) (a) Tang, C.; Jiao, N. Copper-catalyzed aerobic oxidative C-C bond cleavage for C-N bond formation: from ketones to amides. *Angew. Chem., Int. Ed.* **2014**, *53*, 6528−6532. (b) Huang, X.; Li, X.; Zou, M.; Song, S.; Tang, C.; Yuan, Y.; Jiao, N. From Ketones to Esters by a Cu-Catalyzed Highly Selective C(CO)−C(alkyl) Bond Cleavage: Aerobic Oxidation and Oxygenation with Air. *J. Am. Chem. Soc.* **2014**, *136*, 14858−14865.

(14) Li, H.; Li, W.; Liu, W.; He, Z.; Li, Z. An efficient and general iron-catalyzed C-C bond activation with 1,3-dicarbonyl units as a leaving groups. *Angew. Chem., Int. Ed.* **2011**, *50*, 2975−2978.

(15) (a) Maleckis, A.; Sanford, M. S. Catalytic Cycle for Palladium-Catalyzed Decarbonylative Trifluoromethylation using Trifluoroacetic Esters as the CF_3 Source. *Organometallics* **2014**, *33*, 2653−2660. (b) Maleckis, A.; Sanford, M. S. Synthesis of Fluoroalkyl Palladium and Nickel Complexes via Decarbonylation of Acylmetal Species. *Organometallics* **2014**, *33*, 3831−3839.

(16) (a) Jones, J. H. The Cativa Process for the Manufacture of Acetic Acid. *Platinum Metals Rev.* **2000**, *44*, 94−105. (b) Sunley, G. J.; Watson, D. J. High productivity methanol carbonylation catalysis using iridium - The Cativa process for the manufacture of acetic acid. *Catal. Today* **2000**, *58*, 293−307.

(17) For a selective review, see: Shi, W.; Lei, A. 1,3-Diyne chemistry: synthesis and derivations. *Tetrahedron Lett.* **2014**, *55*, 2763−2772.

(18) For a review on Cu(III) intermediates, see: Casitas, A.; Ribas, X. The role of organometallic copper(III) complexes in homogeneous catalysis. *Chem. Sci.* **2013**, *4*, 2301−2318.

(19) As indicated by one of the reviewers, the alkynyl-Cu(I) species which were initially proposed by a reductive elimination of the Cu(III) intermediate might not be the true intermediate, and monoalkynyl-Cu(II) might be the real intermediate according to the control experiments.

(20) Fomina, L.; Vazquez, B.; Tkatchouk, E.; Fomine, S. The Glaser reaction mechanism. A DFT study. *Tetrahedron* **2002**, *58*, 6741−6747.

(21) (a) Mishra, A.; Ma, C. Q.; Bäuerle, P. Functional Oligothiophenes: Molecular Design for Multidimensional Nanoarchitectures and Their Applications. *Chem. Rev.* **2009**, *109*, 1141−1276. (b) Gao, J.; Li, L.; Meng, Q.; Li, R.; Jiang, H.; Li, H.; Hu, W. Dibenzothiophene derivatives as new prototype semiconductors for organic field-effect transistors. *J. Mater. Chem.* **2007**, *17*, 1421−1426. (c) Roncali, J.; Leriche, P.; Cravino, A. From One- to Three-Dimensional Organic Semiconductors: In Search of the Organic Silicon? *Adv. Mater.* **2007**, *19*, 2045−2060.

(22) 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 NaOtBu. *Org. Lett.* **2014**, *16*, 6156−6159.