OL Organic Letters

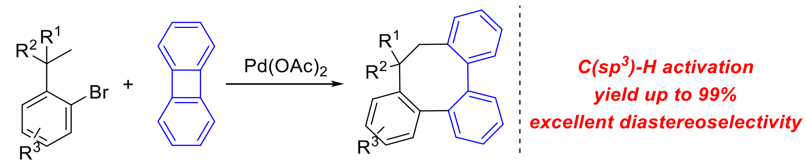
pubs.acs.org/OrgLett Letter

Diastereoselective Construction of Eight-Membered Carbocycles through Palladium-Catalyzed C(sp^3)−H Functionalization

Bin Wan, Zhuoer Lu, Zhuo Wu, Cang Cheng, and Yanghui Zhang*

Cite This: *Org. Lett.* 2021, 23, 1269−1274 Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information



C(sp^3)-H activation
yield up to 99%
excellent diastereoselectivity

A new strategy for the construction of eight-membered carbocycles
A novel chiral scaffold

ABSTRACT: A palladium-catalyzed cross-coupling reaction of 2-alkylphenyl bromides with biphenylene has been developed. The reactions formed eight-membered carbocycles through C(sp^3)−H activation and the formation of two C−C bonds, and the chiral products were obtained with excellent diastereoselectivity. The reaction provides a new strategy for the construction of eight-membered carbocycles, and the products represent a novel type of chiral scaffold.

Eight-membered carbocycles are essential structural motifs that are ubiquitous in natural products, and the majority of these natural cyclooctanoid compounds exhibit important biological and medicinal properties (Figure 1).[1] For instance, taxol is one of the most potent anticancer drugs, and it is being extensively used to treat a variety of human cancers.[2] Notably, dibenzocyclooctadiene lignans, a main subclass of lignans, are eight-membered carbocycles containing a chiral biaryl axis.[3] This class of natural products has been found to exhibit a wide variety of biological activities.[3c] However, methods for the construction of eight-membered carbocycles are still limited, and most of the current methods involve intramolecular cyclization from acyclic precursors.[4] These methods are usually challenging due to the unfavorable entropy effect and transannular interactions.[1a] Furthermore, the acyclic precursors essentially have the same level of structural complexity as the carbocycles to be synthesized; therefore, the syntheses of the precursors typically require multisteps. This challenge can be addressed by intermolecular reactions, which may start from relatively simple starting materials. Although some intermolecular cycloaddition reactions have been developed for the synthesis of eight-membered carbocycles, they are primarily limited to the reactions of alkenes and alkynes, which restricts

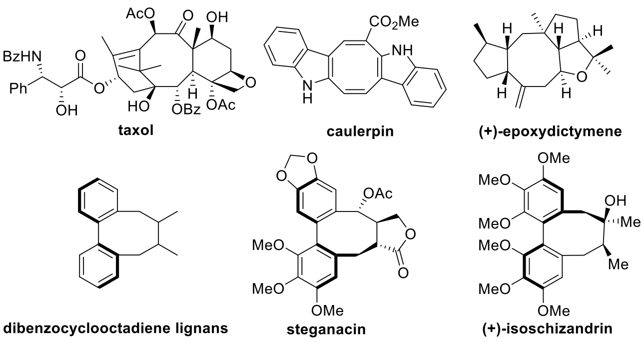
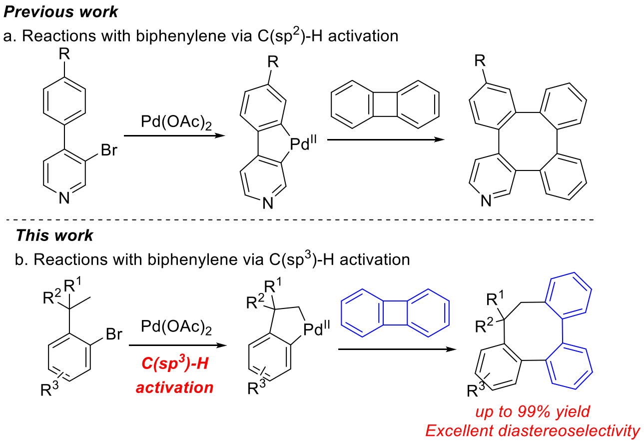


Figure 1. Representative natural products containing eight-membered carbocycles.

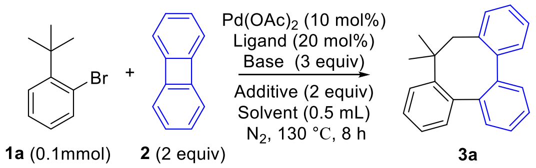
Scheme 1. Reactions of Aryl Bromides with Biphenylene



Received: December 23, 2020
Published: February 9, 2021

https://dx.doi.org/10.1021/acs.orglett.0c04244

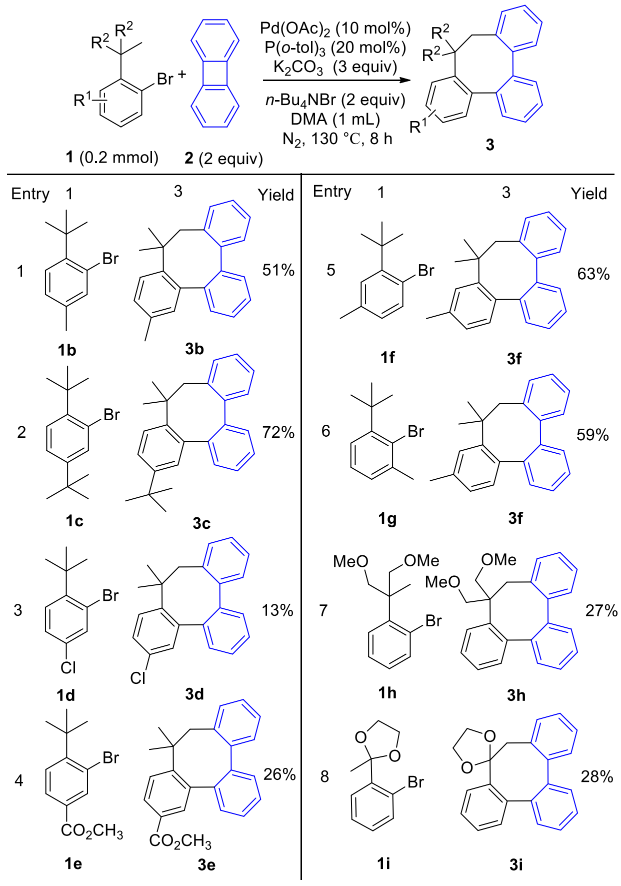
Table 1. Optimization of Reaction Conditions[a]



entry	base	ligand	additive	solvent	yield (%)
1	**K_2CO_3**	**P(*o*-tol)$_3$**	***n*-Bu_4NBr**	**DMA**	70
2	K_2CO_3	P(*o*-tol)$_3$		DMA	56
3	K_2CO_3	P(*o*-tol)$_3$	*n*-Bu_4NCl	DMA	54
4	K_2CO_3		*n*-Bu_4NBr	DMA	48
5	K_2CO_3	PPh_3	*n*-Bu_4NBr	DMA	33
6	K_2CO_3	P(*p*-tol)$_3$	*n*-Bu_4NBr	DMA	47
7	K_2CO_3	PCy3	*n*-Bu_4NBr	DMA	28
8	Na_2CO_3	P(*o*-tol)$_3$	*n*-Bu_4NBr	DMA	50
9	Cs_2CO_3	P(*o*-tol)$_3$	*n*-Bu_4NBr	DMA	53
10	KOAc	P(*o*-tol)$_3$	*n*-Bu_4NBr	DMA	60
11	K_3PO_4	P(*o*-tol)$_3$	*n*-Bu_4NBr	DMA	52
12	K_2CO_3	P(*o*-tol)$_3$	*n*-Bu_4NBr	DMF	67
13	K_2CO_3	P(*o*-tol)$_3$	*n*-Bu_4NBr	NMP	51
14	K_2CO_3	P(*o*-tol)$_3$	*n*-Bu_4NBr	1,4-dioxane	NR
15	K_2CO_3	P(*o*-tol)$_3$	*n*-Bu_4NBr	CH_3CN	50
16[b]	K_2CO_3	P(*o*-tol)$_3$	*n*-Bu_4NBr	DMF	64

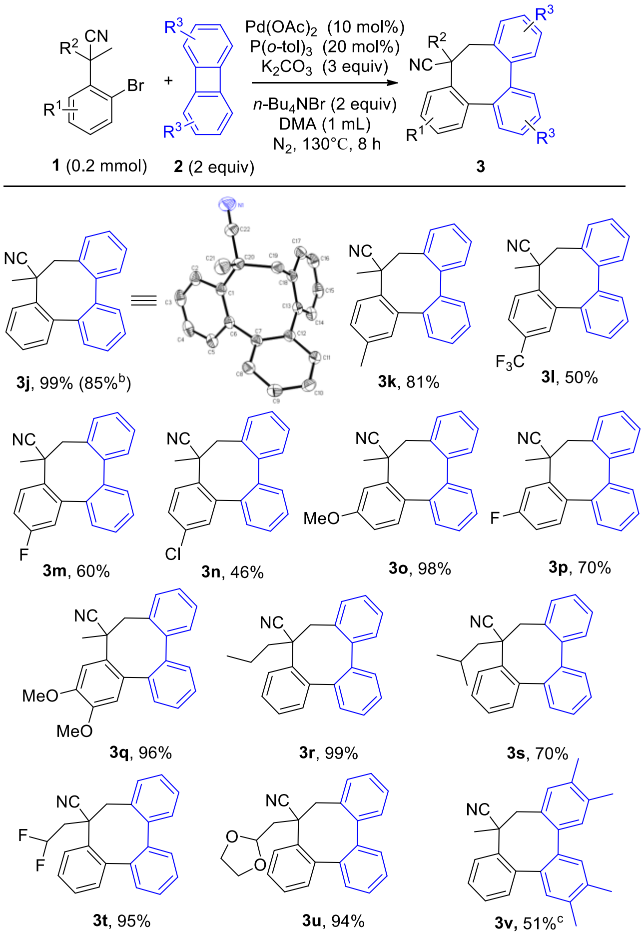
[a] Yields were determined by ^1H NMR analysis of the crude reaction mixture using CH_2Br_2 as the internal standard. [b] 5 mol % $Pd(OAc)_2$ and 10% P(*o*-tol)$_3$

Scheme 2. Substrate Scope[a]



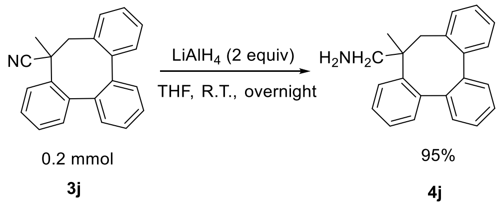
[a] Isolated yield

Scheme 3. Diastereoselective Synthesis of Chiral Eight-Membered Carbocycles[a]



[a] Isolated yield. [b] 1 mmol of **1j** was used. [c] 0.1 mmol of **1j** and 0.1 mmol of 2,3,6,7-tetramethylbiphenylene were used.

Scheme 4. Transformation of Cyano Groups

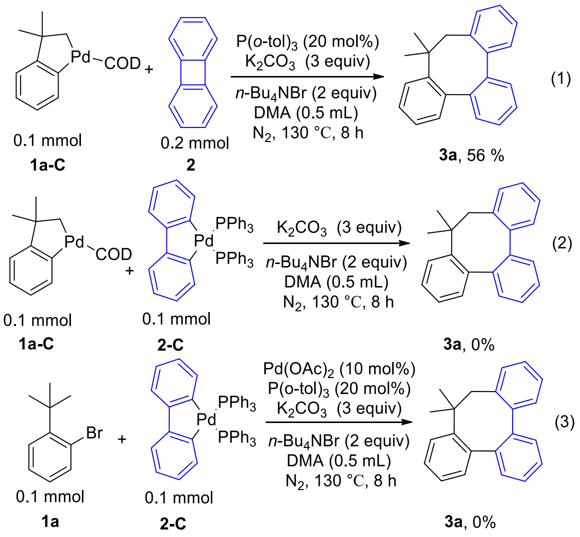


the scope of accessible products.[1b,5] Therefore, it is still highly desirable to develop new synthetic strategies for eight-membered carbocycles, in particular, those through intermolecular reactions.

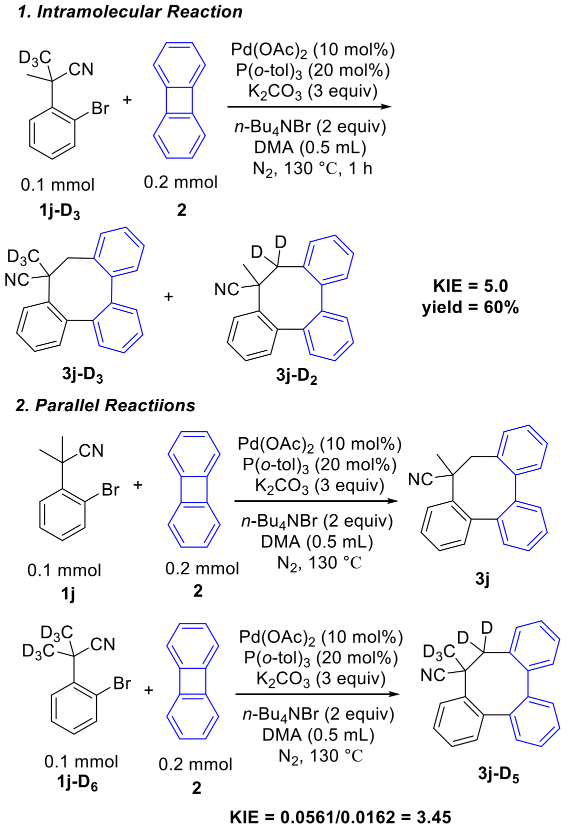
C−H functionalization represents an innovative tactic for organic synthesis.[6] Whereas C(sp^2)−H activation reactions have been extensively exploited, C(sp^3)−H functionalization is still underdeveloped because it is more challenging.[7]

Directing groups are often used to achieve high regioselectivity in transition-metal-catalyzed C−H functionalization reactions.[8] However, this strategy needs additional steps to introduce and transform the directing groups. Remarkably, halogens have been exploited as traceless directing groups to assist the cleavage of C−H bonds. For Pd-catalyzed halogen-assisted C−H activation reactions, C,C-

Scheme 5. Mechanistic Studies

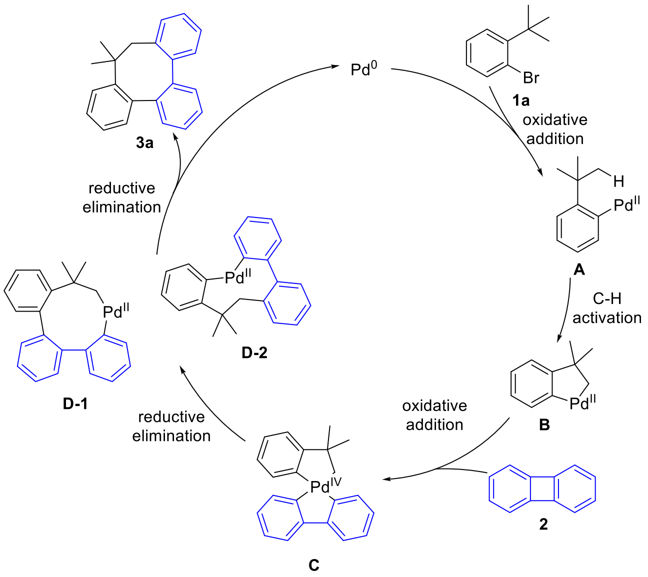


Scheme 6. Kinetic Isotope Effect Studies



palladacycles are formed.[9] Our group has a long-standing interest in palladacycles because their unique structures and novel reactivities can be utilized to develop innovative and synthetically useful organic transformations.[10] Notably, Pd-catalyzed C(sp^3)−H activation can also be enabled by utilizing halogens as traceless directing groups, which forms C(sp^2),C(sp^3)-palladacycles. The majority of the current C(sp^3)−H activation reactions of such type involve intramolecular cyclization,[11] and intermolecular functionalization is underexploited.[10,12]

Scheme 7. Proposed Mechanism



In 2006, the Gallagher group reported a very intriguing cross-coupling reaction of 2-4-aryl-3-bromopyridines with biphenylene (Scheme 1a).[13] The reactions involved C(sp^2),C(sp^2)-palladacycles obtained from bromo-directed C(sp^2)−H activation and formed eight-membered heterocyclic tetraphenylenes. Although only three examples were studied and the yields were low in Gallagher's reactions, the reactions provided a strategy for the construction of eight-membered rings. Inspired by this elegant reaction, we envisioned that C(sp^2),C(sp^3)-palladacycles derived by the C(sp^3)−H activation of aryl halides could also undergo a coupling reaction with biphenylene. However, C(sp^3)−H activation is more challenging, and it has also been reported that aryl halides tend to undergo homocoupling via Pd-catalyzed C(sp^3)−H activation.[14] To develop the cross-coupling of C(sp^3)−H bonds of aryl halides with biphenylene, these challenges have to be addressed. Herein we report the cross-coupling reaction of aryl bromides and biphenylene via C(sp^3)−H activation. This reaction represents an innovative method for the diastereoslective construction of eight-membered carbocycles (Scheme 1b).

We first investigated the reaction of 1-bromo-2-(*tert*-butyl)benzene (**1a**) and biphenylene (**2**). After an extensive conditions survey, we obtained the desired eight-membered product **3a** in 70% yield under the conditions shown in Table 1 (entry 1). Removing *n*-Bu_4NBr or using *n*-Bu_4NCl led to a lower yield (entries 2 and 3). The yield also decreased in the absence of P(*o*-tol)$_3$ or in the presence of other phosphine ligands (entries 4−7). The survey of other inorganic bases revealed that K_2CO_3 was the optimal base (entries 8−11). Furthermore, the reaction proceeded less efficiently in DMF, NMP, and CH_3CN and failed to give **3a** in 1,4-dioxane (entries 12−15). Notably, a yield of 64% was still obtained using 5 mol % of Pd(OAc)$_2$ and 10 mol % of P(*o*-tol)$_3$ (entry 16).

Having identified the optimal conditions for the synthesis of eight-membered carbocycles, we investigated the substrate scope of the cross-coupling reaction. The reactions of 1-bromo-2-(*tert*-butyl)benzene derivatives were first probed. As shown in Scheme 2, the substrates bearing a methyl or *tert*-butyl group at the five-position generated the corresponding products in moderate yields (**3b** and **3c**). A chloro group was tolerated, yet the yield was low (**3d**). The substrate bearing an electron-withdrawing ester group was also suitable, but the reaction was low-yielding (**3e**). Intriguingly, four- or six-substituted substrates (**1f** and **1g**) gave the same product **3f**. The formation of **3f** in the reaction of **1g** should be caused by palladium migration. (For the detailed mechanism, see the Supporting Information.) Whereas the activated C(sp^3)−H bonds are from *tert*-butyl groups for the above substrates, the reactivity of C(sp^3)−H bonds from other groups was also examined. Gratifyingly, bromobenzenes bearing a dimethoxy-substituted *tert*-butyl group or a 1,3-dioxolanyl group also successfully coupled to biphenylene, albeit in low yields (**3h** and **3i**).

It is noted that the previously mentioned eight-membered carbocycle products are chiral. Actually, product **3a** contains two enantiomers, and they are separable by HPLC. (See the Supporting Information.) The eight-membered carbocycle represents a novel type of chiral skeleton and may find applications in various fields such as asymmetric synthesis and materials science. For example, dibenzocyclooctadiene lignans are chiral eight-membered carbocycles.[3] Therefore, we set out to study the stereoselectivity of the cross-coupling reaction. We first examined the reaction of 1-bromo-2-(2-cyano-isopropyl)-benzene (**1j**). Substrate **1j** bears two methyl groups. When one of the two methyl groups is functionalized, a new chiral centers will be created. Remarkably, **1j** reacted with **2** under the standard conditions to form the eight-membered product **3j** in quantitative yield (Scheme 3). More intriguingly, the reaction was highly diastereoselective, and only a pair of enantiomers was obtained. The two enantiomers of **3j** were also separable by HPLC (see the Supporting Information), and the structure of **3j** was identified by single-crystal X-ray crystallography. The molecule has a very intriguing structure. The two opposite benzene rings are located above the average plane of the eight-membered ring, and the other benzene ring is below the plane. Next, the reactions of the derivatives of **1j** were probed (Scheme 3). The derivatives bearing an electron-donating methyl or electron-withdrawing trifluoromethyl group at the position meta to the bromo group were suitable (**3k** and **3l**). Although the yields decreased, the diastereoselectivities were still excellent. Both fluoro and chloro groups were tolerated, yet the reactions were far lower yielding (**3m** and **3n**). Para- and disubstituted derivatives were also reactive, and the corresponding products were formed in good or excellent yields (**3o**−**3q**). In these reactions, only enantiomers were obtained. When chiral substrates were used, the reactions were still highly diastereoselective, forming a pair of enantiomers in almost quantitative yields (**3r**−**3u**). Notably, the yield of the reaction of **1j** and 2,3,6,7-tetramethylbiphenylene was moderate, and only enantiomers were obtained (**3v**).

The cyano group could be transformed in multiple ways. For instance, it could be reduced to an amino group (Scheme 4). The amino group can be readily manipulated to allow for further functionalization.

Mechanistically, it has been proposed that palladacycle Pd(2,2′-biaryl)s could react with biphenylene to form tetraphenylenes in the cross-coupling of 3-bromo-4-phenyl-pyridines with biphenylene and the homocoupling of biphenylene.[13,15] However, the coupling of C(sp^2),C(sp^3)-palladacycles with biphenylene has not been reported. To obtain evidence to support the notion that palladacycles also acted as the intermediates in the coupling reaction of C(sp^3)−H bonds with biphenylenes, we prepared palladacycle **1a-C**. **1a-C** could react with biphenylene to form product **3a** (Scheme 5, reaction 1). Furthermore, it has been reported that Ni(2,2-biphenyl) tends to undergo homocoupling to form tetraphenylene.[16] To examine if the reactions involved the cross-coupling of two palladacycles, we also prepared complex **2-C**. When palladacycle **1a-C** was allowed to react with **2-C**, product **3a** was not observed (reaction 2). Complex **2-C** also failed to react with **1a** (reaction 3). Although the cross-coupling of two palladacycles could not be excluded, these experimental results support the notion that C(sp^2),C(sp^3)-palladacycles were the intermediates and they reacted with biphenylene to generate eight-membered carbocycle products.

Kinetic isotope effects (KIEs) in the reaction were also studied. Deuterated substrates **1j-D$_3$** and **1j-D$_6$** were prepared. When **1j-D$_3$** was subjected to the standard conditions, products **3j-D$_3$** and **3j-D$_2$** were obtained in a ratio of 5.0 to 1, which indicates that the intramolecular KIE is 5.0. Furthermore, parallel reactions of **3j** and **3j-D$_6$** were conducted. **3j** and **3j-D$_6$** were allowed to react with **2**, respectively, under standard conditions for different periods of time, and the KIE value was obtained as 3.45 (Scheme 6). These KIE values imply that C(sp^3)−H activation should be the rate-determining step.

Therefore, a mechanism was proposed for the formation of **3a** (Scheme 7). The reaction is initiated by the oxidative addition of **1a** to Pd^0 species, which yields Pd^{II} species **A**. The Pd^{II} species activates the C(sp^3)−H bond to form palladacycle **B**. The oxidative addition of biphenylene **2** to palladacycle **B** affords Pd^{IV} species **C**. The subsequent reductive elimination of Pd^{IV} species **C** gives two possible nine-membered palladacycles **D-1** and **D-2**. Finally, a second reductive elimination generates product **3a** and the Pd^0 species.

In conclusion, we have developed a palladium-catalyzed cross-coupling reaction of 2-alkylphenyl bromides with biphenylene through C(sp^3)−H activation. The reaction forms eight-membered carbocycles as the products with excellent diastereoselectivity. Mechanistic studies revealed that palladacycles formed by C(sp^3)−H activation should act as the key intermediates. The reaction provides an innovative strategy for the synthesis of eight-membered carbocycles, and the products represent a novel type of chiral scaffold.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c04244.

> Detailed experimental procedures, crystallographic data of compound 3j, HPLC data of compounds 3a and 3j, and characterization data and NMR spectra of all products and new substrate (PDF)

Accession Codes

CCDC 2045337 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

Yanghui Zhang − *School of Chemical Science and Engineering, Shanghai Key Laboratory of Chemical Assessment and Sustainability, Tongji University, Shanghai 200092, P. R. China;* orcid.org/0000-0003-2189-3496; Email: zhangyanghui@tongji.edu.cn

Authors

Bin Wan − *School of Chemical Science and Engineering, Shanghai Key Laboratory of Chemical Assessment and Sustainability, Tongji University, Shanghai 200092, P. R. China*

Zhuoer Lu − *School of Chemical Science and Engineering, Shanghai Key Laboratory of Chemical Assessment and Sustainability, Tongji University, Shanghai 200092, P. R. China*

Zhuo Wu − *School of Chemical Science and Engineering, Shanghai Key Laboratory of Chemical Assessment and Sustainability, Tongji University, Shanghai 200092, P. R. China*

Cang Cheng − *School of Chemical Science and Engineering, Shanghai Key Laboratory of Chemical Assessment and Sustainability, Tongji University, Shanghai 200092, P. R. China*

Complete contact information is available at:
https://pubs.acs.org/10.1021/acs.orglett.0c04244

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

The work was supported by the National Natural Science Foundation of China (nos. 21971196 and 21672162) and the Shanghai Science and Technology Commission (14DZ2261100).

REFERENCES

(1) (a) Hu, Y.-J.; Li, L.-X.; Han, J.-C.; Min, L.; Li, C.-C. *Chem. Rev.* **2020**, *120*, 5910−5953. (b) Yu, Z.-X.; Wang, Y.; Wang, Y.-Y. *Chem. - Asian J.* **2010**, *5*, 1072−1088. (c) Faulkner, D. J. *Nat. Prod. Rep.* **1988**, *5*, 613−663.

(2) (a) Suffness, M. *Taxol: Science and Applications*; CRC Press: Boca Raton, FL, 1995. (b) Kingston, D. G. I. *J. Org. Chem.* **2008**, *73*, 3975−3984.

(3) (a) Chang, J.-B.; Reiner, J.; Xie, J.-X. *Chem. Rev.* **2005**, *105*, 4581−4609. (b) Fang, X.-H.; Hu, X.-D. *Molecules* **2018**, *23*, 3385. (c) Gao, X.-M.; Wang, R.-R.; Niu, D.-Y.; Meng, C.-Y.; Yang, L.-M.; Zheng, Y.-T.; Yang, G.-Y.; Hu, Q.-F.; Sun, H.-D.; Xiao, W.-L. *J. Nat. Prod.* **2013**, *76*, 1052−1057.

(4) (a) Mehta, G.; Singh, V. *Chem. Rev.* **1999**, *99*, 881−930. (b) Michaut, A.; Rodriguez, J. *Angew. Chem., Int. Ed.* **2006**, *45*, 5740−5750. (c) Yet, L. *Chem. Rev.* **2000**, *100*, 2963−3007. (d) Petasis, N. A.; Patane, M. A. *Tetrahedron* **1992**, *48*, 5757−5821. (e) Wang, Y.; Yu, Z.-X. *Acc. Chem. Res.* **2015**, *48*, 2288−2296.

(5) (a) Fu, X.-F.; Xiang, Y.; Yu, Z.-X. *Chem. - Eur. J.* **2015**, *21*, 4242−4246. (b) Zhang, L.; Wang, Y.; Yao, Z.-J.; Wang, S.-Z.; Yu, Z.-X. *J. Am. Chem. Soc.* **2015**, *137*, 13290−13300. (c) Juliá-Hernández, F.; Ziadi, A.; Nishimura, A.; Martin, R. *Angew. Chem., Int. Ed.* **2015**, *54*, 9537−9541. (d) Yang, S.; Xu, Y.; Li, J. *Org. Lett.* **2016**, *18*, 6244. (e) Kennedy, C. R.; Zhong, H. Y.; Macaulay, R. L.; Chirik, P. J. *J. Am. Chem. Soc.* **2019**, *141*, 8557−8573. (f) Braconi, E.; Götzinger, A. C.; Cramer, N. *J. Am. Chem. Soc.* **2020**, *142*, 19819−19842.

(6) (a) *C−H Activation*; Yu, J.-Q., Shi, Z., Eds.; Springer: Heidelberg, Germany, 2010. (b) Zhang, Y.-H.; Shi, G.-F.; Yu, J.-Q. Carbon-Carbon-Bond Formation via C−H Bond Functionalization. In *Comprehensive Organic Synthesis*, 2nd ed.; Molander, G., Knochel, P., Eds.; Elsevier: Oxford, U.K., 2014; Vol. 3, pp 1101−1209. (c) Liu, C.; Yuan, J.-W.; Gao, M.; Tang, S.; Li, W.; Shi, R.-Y.; Lei, A.-W. *Chem. Rev.* **2015**, *115*, 12138−12204. (d) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147−1169. (e) Daugulis, O.; Roane, J.; Tran, L. D. *Acc. Chem. Res.* **2015**, *48*, 1053−1064. (f) Miao, J.; Ge, H. *Eur. J. Org. Chem.* **2015**, *2015*, 7859−7868. (g) Gensch, T.; Hopkinson, M. N.; Glorius, F.; Wencel-Delord, J. *Chem. Soc. Rev.* **2016**, *45*, 2900−2936. (h) Moselage, M.; Li, J.; Ackermann, L. *ACS Catal.* **2016**, *6*, 498−525. (i) Zhang, Q.; Shi, B.-F. *Chin. J. Chem.* **2019**, *37*, 647−656. (j) Rej, S.; Ano, Y.; Chatani, N. *Chem. Rev.* **2020**, *120*, 1788−1887.

(7) (a) He, J.; Wasa, M.; Chan, K. S. L.; Shao, Q.; Yu, J.-Q. *Chem. Rev.* **2017**, *117*, 8754−8786. (b) Xu, Y.; Dong, G.-B. *Chem. Sci.* **2018**, *9*, 1424−1432. (c) Chen, Z.; Rong, M.-Y.; Nie, J.; Zhu, X.-F.; Shi, B.-F.; Ma, J.-A. *Chem. Soc. Rev.* **2019**, *48*, 4921−4942. (d) Li, B.-J.; Shi, Z.-J. *Chem. Soc. Rev.* **2012**, *41*, 5588−5598. (e) Chu, J. C. K.; Rovis, T. *Angew. Chem., Int. Ed.* **2018**, *57*, 62−101. (f) Jazzar, R.; Hitce, J.; Renaudat, A.; Sofack-Kreutzer, J.; Baudoin, O. *Chem. - Eur. J.* **2010**, *16*, 2654−2672. (g) He, G.; Wang, B.; Nack, W. A.; Chen, G. *Acc. Chem. Res.* **2016**, *49*, 635−645.

(8) (a) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147−1169. (b) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788−802. (c) Rousseau, G.; Breit, B. *Angew. Chem., Int. Ed.* **2011**, *50*, 2450−2494. (d) Zhang, F. Z.; Spring, D. R. *Chem. Soc. Rev.* **2014**, *43*, 6906−6919. (e) Chen, Z.-K.; Wang, B.-J.; Zhang, J.-T.; Yu, W.-L.; Liu, Z.-X.; Zhang, Y.-L. *Org. Chem. Front.* **2015**, *2*, 1107−1295. (f) Huang, Z.-X.; Lim, H.-N.; Mo, F.-Y.; Young, M. C.; Dong, G.-B. *Chem. Soc. Rev.* **2015**, *44*, 7764−7786.

(9) (a) Campo, M. A.; Huang, Q.; Yao, T.; Tian, Q.; Larock, R. C. *J. Am. Chem. Soc.* **2003**, *125*, 11506−11507. (b) Hennessy, E. J.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 12084−12085. (c) Garcia-Cuadrado, D.; Braga, A. A. C.; Maseras, F.; Echavarren, A. M. *J. Am. Chem. Soc.* **2006**, *128*, 1066−1067. (d) Campeau, L. C.; Parisien, M.; Jean, A.; Fagnou, K. *J. Am. Chem. Soc.* **2006**, *128*, 581−590. (e) Garcia-Cuadrado, D.; de Mendoza, P.; Braga, A. A. C.; Maseras, F.; Echavarren, A. M. *J. Am. Chem. Soc.* **2007**, *129*, 6880−6886. (f) Albicker, M. R.; Cramer, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 9139−9142. (g) Shintani, R.; Otomo, H.; Ota, K.; Hayashi, T. *J. Am. Chem. Soc.* **2012**, *134*, 7305−7308. (h) Gao, D.-W.; Yin, Q.; Gu, Q.; You, S.-L. *J. Am. Chem. Soc.* **2014**, *136*, 4841−4844. (i) Deng, R.; Huang, Y.; Ma, X.; Li, G.; Zhu, R.; Wang, B.; Kang, Y.-B.; Gu, Z. *J. Am. Chem. Soc.* **2014**, *136*, 4472−4475. (j) Sickert, M.; Weinstabl, H.; Peters, B.; Hou, X.; Lautens, M. *Angew. Chem., Int. Ed.* **2014**, *53*, 5147−5151. (k) Yang, Y.; Zhou, B.; Zhu, X.; Deng, G.; Liang, Y.; Yang, Y. *Org. Lett.* **2018**, *20*, 5402−5405.

(10) (a) Wu, Z.; Ma, D.; Zhou, B.; Ji, X.-M.; Ma, X.-T.; Wang, X.-L.; Zhang, Y.-H. *Angew. Chem., Int. Ed.* **2017**, *56*, 12288−12291. (b) Lu, A.-L.; Ji, X.-M.; Zhou, B.; Wu, Z.; Zhang, Y.-H. *Angew. Chem., Int. Ed.* **2018**, *57*, 3233−3237. (c) Sun, X.-L.; Wu, Z.; Qi, W.-X.; Ji, X.-M.; Cheng, C.; Zhang, Y.-H. *Org. Lett.* **2019**, *21*, 6508−6512. (d) Gu, Y.-C.; Sun, X.-L.; Wan, B.; Lu, Z.-E.; Zhang, Y.-H. *Chem. Commun.* **2020**, *56*, 10942−10945.

(11) (a) Baudoin, O. *Acc. Chem. Res.* **2017**, *50*, 1114−1123. (b) Dyker, G. *Angew. Chem., Int. Ed.* **1999**, *38*, 1698−1712. (c) Chaumontet, M.; Piccardi, R.; Audic, N.; Hitce, J.; Peglion, J. L.; Clot, E.; Baudoin, O. *J. Am. Chem. Soc.* **2008**, *130*, 15157−15166. (d) Rousseaux, S.; Davi, M.; Sofack-Kreutzer, J.; Pierre, C.; Kefalidis, C. E.; Clot, E.; Fagnou, K.; Baudoin, O. *J. Am. Chem. Soc.* **2010**, *132*, 10706−10716. (e) Yan, J.-X.; Li, H.; Liu, X.-W.; Shi, J.-L.; Wang, X.; Shi, Z.-J. *Angew. Chem.* **2014**, *126*, 5045−5049. (f) Wang, M.; Zhang, X.; Zhuang, Y.-X.; Xu, Y.-H.; Loh, T.-P. *J. Am. Chem. Soc.* **2015**, *137*, 1341−1347.

(12) (a) Gutiérrez-Bonet, Á.; Juliá-Hernández, F.; de Luis, B.; Martin, R. *J. Am. Chem. Soc.* **2016**, *138*, 6384−6387. (b) Tan, B.-J.; Bai, L.; Ding, P.; Liu, J.-J.; Wang, Y.-Y.; Luan, X.-J. *Angew. Chem.*

2018, *131*, 1488−1492. (c) Cai, S.-L.; Li, Y.; Yang, C.; Sheng, J.; Wang, X.-S. *ACS Catal.* **2019**, *9*, 10299−10304.

(13) Masselot, D.; Charmant, J. P. H.; Gallagher, T. *J. Am. Chem. Soc.* **2006**, *128*, 694−695.

(14) (a) Dyker, G. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1023−1025. (b) Dyker, G. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 103−105.

(15) Edelbach, B. L.; Lachicotte, R. J.; Jones, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 2843−2853.

(16) (a) Eisch, J. J.; Piotrowski, A. M.; Han, K. I.; Krüger, C.; Tsay, Y. H. *Organometallics* **1985**, *4*, 224−231. (b) Lu, Z.; Jun, C.-H.; de Gala, S. R.; Sigalas, M. P.; Eisenstein, O.; Crabtree, R. H. *Organometallics* **1995**, *14*, 1168−1175. (c) Perthuisot, C.; Edelbach, B. E.; Zubris, D. L.; Jones, W. D. *Organometallics* **1997**, *16*, 2016−2023.