Organic LETTERS

Letter

pubs.acs.org/OrgLett

Palladium(0)-Catalyzed Methylcyclopropanation of Norbornenes with Vinyl Bromides and Mechanism Study

Jiangang Mao,[†,‡] Hujun Xie,[§] and Weiliang Bao*[,†]

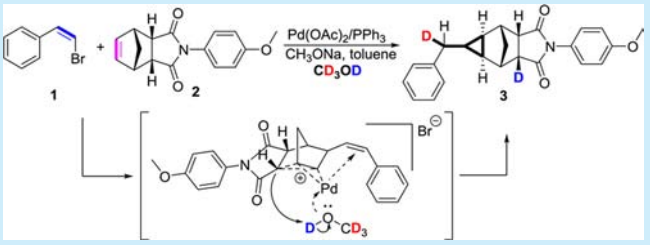
[†]Department of Chemistry, Zhejiang University, Hangzhou 310028, Zhejiang, P.R. China

[‡]School of Metallurgy and Chemical Engineering, Jiangxi University of Science and Technology, Ganzhou 341000, Jiangxi, P.R. China

[§]School of Food Science and Biotechnology, Zhejiang Gongshang University, Hangzhou 310035, Zhejiang P.R. China

Supporting Information

ABSTRACT: An unusual methylcyclopropanation from [2 + 1] cycloadditions of vinyl bromides to norbornenes catalyzed by $Pd(OAc)_2/PPh_3$ in the presence of CH_3ONa and CH_3OH has been established. A methylcyclopropane subunit was installed by a 3-fold domino procedure involving a key protonation course. Preliminary deuterium-labeling studies revealed that the proton came from methyl of CH_3OH and also exposed an additional hydrogen/deuterium exchange process. These two proton-concerned reactions were fully chemoselective.

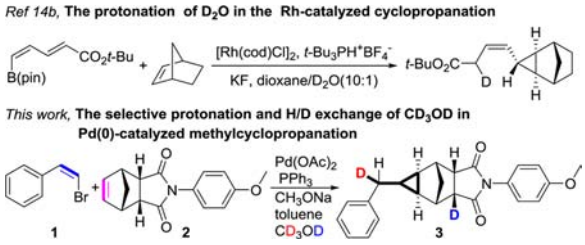


As a significant structural motif, the cyclopropane skeleton is found in numerous biomolecules and pharmaceutical drugs, such as pyrethrum,[1] FR-900848,[2] lactobacillic acid,[3] and tranylcypromine.[4] Cyclopropanation is always a highly active area of organic chemistry for both theoretical and practical purposes[5] and has attracted tremendously attention from organic chemists. Among the myriad methods available for constructing the cyclopropane scaffold,[5,6] transition-metal-catalyzed C−H or C−C bond activation is undoubtedly a fascinating methodology,[7] except for carbene/carbenoid cycloaddition,[8] Simmons−Smith reaction,[9] Michael-initiated ring closure (MIRC),[10] and cycloisomerization.[11] The cyclopropanation via the coupling of norbornenes with organoboron reagents or alkynes has been reported.[12] The intermolecular cyclopropanation of halohydrocarbon generally underwent a carbene intermediate.[8a,b] However, transition-metal-catalyzed cyclopropanation of halohydrocarbon with alkenes via a noncarbene mechanism remains underdeveloped.[13] Herein, we report the first example of $Pd(OAc)_2/PPh_3$-catalyzed methylcyclopropanation of bromostyrenes with norbornenes via [2 + 1] cycloaddition involving a methylene protonation and an additional H/D exchange with CD_3OD (Scheme 1).

In a few cases, the protonation reaction was accompanied by transition-metal-catalyzed coupling reactions. The proton sources may be materials such as alcohol and water, etc.[14] The alkoxy group of alcohol can afford a proton via coordination with transition metal,[15] and hydroxyl can also initiate an H/D exchange by transition-metal-catalyzed C−H activation.[16] However, to the best of our knowledge, transition-metal-catalyzed coupling reactions involving both protonation and H/D exchange reactions have not been reported.

The Pd(0)-catalyzed methylenecyclopropanation and bismethenylcyclobutanation of bromostyrenes with norbornenes were

Scheme 1. Protonation and H/D Exchange in Transition-Metal-Catalyzed Coupling Reaction



carried out successfully using K_2CO_3 and Cs_2CO_3 as base, respectively, in our laboratory.[13a,17] While further studying the selectivity of the above reactions, we found methylcyclopropane product in the presence of CH_3ONa as base. The preliminary evaluation on this result revealed that the norbornenylpalladium imtermediate grabbed a proton from the reaction system. However, subsequent reaction mechanism research demonstrated that the methylcyclopropanation process underwent a protonation and an additional H/D exchange with CD_3OD. Two kinds of deuterium atoms from CD_3OD were all embedded chemoselectively in the different positions of norbornene-fused methylcyclopropane derivatives (Scheme 1).

The interesting domino [2 + 1] cycloaddition reaction prompted us to investigate the reaction parameters. (*Z*)-1-(2-Bromovinyl)-4-methoxybenzene **1a** and *endo*-*N*-(*p*-tolyl)-norbornenesuccinimide **2a** were employed as model substrates to optimize the reaction conditions. The results are summarized in the Supporting Information (Table SI1). Previous studies

Received: June 1, 2015
Published: July 21, 2015

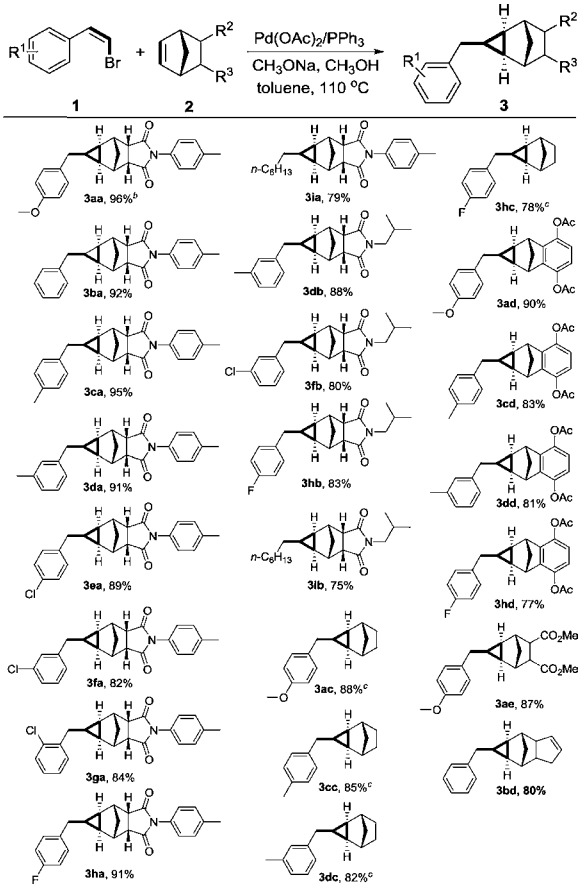
DOI: 10.1021/acs.orglett.5b01603
Org. Lett. 2015, 17, 3678−3681

showed that base was a key reaction parameter, so different bases such as K_2CO_3, Cs_2CO_3, CsOAc, C_2H_5ONa, and CH_3ONa were reviewed first. It affected both product yields and product categories. When 2.0 and 3.0 equiv of Cs_2CO_3 was used as base and 0.2 mL of CH_3OH was added, the desired product **3aa** was isolated, respectively, in 31% and 78% yields (see Table SI1, entries 2 and 3). When K_2CO_3 was employed as base, the reaction gave **4aa** as product but not **3aa** (92% yield, Table SI1, entry 1).[13a] Even if 4.0 or 6.0 equiv of CsOAc was used as base, **4aa** was still the main product (72% and 75% yield, Table SI1, entries 4 and 5). C_2H_5ONa afforded 85% yield product **3aa**. The [2 + 1] cycloaddition afforded methylcyclopropane **3aa** with the best yield in the presence of 3.0 equiv of CH_3ONa (96% yield, entry 10).

After CH_3ONa was identified as the best base, other reaction parameters were optimized using it. Several Pd precatalysts were screened (Table SI1, entries 10−13). Using $Pd(dppf)Cl_2$ as the precatalyst, **3aa** was obtained in 83% yield (Table SI1, entry 13), while $PdCl_2$ and $Pd(PPh_3)_4$ delivered the desired products in 52% and 74% yields, respectively (Table SI1, entries 11 and 12). Then the ligands dppe, BINAP, TMOPP, and TCHP were screened and afforded **3aa** in 74%, 70%, 91%, and 68% yields, respectively (Table SI1, entries 6−9). The effects of solvent and additive were also investigated. The reaction could be conducted successfully in methanol (63% yield, Table SI1, entry 18). Other solvents, such as CH_3CN, dioxane, DMSO, and DMF, were also suitable for the reaction but only afforded **3aa** in low or moderate yields (43%−66% yield, Table SI1, entries 14−17). Subsequently, additives such as C_2H_5OH, $PhCH_2OH$, and $Cl(CH_2)_2OH$ were also surveyed; methylcyclopropane **3aa** was obtained in 42%, 61%, and 72% yields, respectively, in the presence of Cs_2CO_3 due to the different pK_a and steric hindrance of the alcohols (Table SI1, entries 21−23). The loading of 1.0 mL of CH_3OH reduced the yield of **3aa** to 75% (Table SI1, entry 20). When the reaction was carried out in the absence of CH_3OH, the result was not ideal and only afforded a trace of the desired product (Table SI1, entry 19). The best reaction temperature is at 110 °C (96% yield, Table SI1, entry 10). The yields decreased to 91% and 66%, respectively, when the reactions were carried out at 120 and 90 °C (Table SI1, entries 24 and 25). The best yield of methylcyclopropane **3aa** was obtained when the model reaction was catalyzed by $Pd(OAc)_2/PPh_3$, 3.0 equiv of CH_3ONa was employed as base, and 0.2 mL of CH_3OH was used as the additive in toluene (96% yield, Table SI1, entry 10).

With the optimized reaction conditions in hand, some representative substrates were employed to investigate the scope and generality of the [2 + 1] cycloaddition domino reaction, as shown in Scheme 2. (*Z*)-2-Bromovinylarenes bearing electron-donating (3-Me, 4-Me, and 4-MeO) groups on the benzene core afforded the corresponding methylcyclopropane derivatives **3** in excellent yields (Scheme 2, **3aa**, **3ca−da**, **3db**, **3ac**, **3cc−dc**, **3ad**, **3cd−dd**), while (*Z*)-2-bromovinylarenes bear-ing electron-withdrawing groups (2-Cl, 3-Cl, 4-Cl, and 4-F) on the benzene ring provided products **3** in good to high yields (Scheme 2, **3ea−ha**, **3fb**, **3hb**, **3hc**, **3hd**). The *para*-substituted vinylarenes provided methylcyclopropane products **3ca**, **3ea**, **3cc**, and **3cd** in higher yield (Scheme 2, 95%, 89%, 85% and 83% yield) owing to much smaller steric hindrance compared with the corresponding *meta*-substituted vinylarenes (**3da**, **3fa**, **3dc**, and **3dd**; 91%, 82%, 82%, and 81% yield). The reaction scope was further extended to aliphatic (*Z*)-1-bromoalkenes **1i** successfully,

Scheme 2. Substrate Scope of Pd-Catalyzed Methylcyclopropanation of Norbornenes with (*Z*)-Vinyl Bromides[a]



[a]Reaction conditions unless otherwise noted: **1** (0.55 mmol), **2** (0.5 mmol), $Pd(OAc)_2$ (0.05 mmol), PPh_3 (0.11 mmol), CH_3ONa (1.5 mmol), toluene (2.0 mL), CH_3OH (0.2 mL), 110 °C, 12 h in sealed tube. Isolated yields are shown. [b]CH_3ONa (1.0 mmol). [c]Reaction conditions: **1** (0.5 mmol), **2** (0.6 mmol), $Pd(OAc)_2$ (0.05 mmol), PPh_3 (0.11 mmol), CH_3ONa (2.0 mmol), toluene (2.0 mL).

and afforded methylcyclopropanation products **3ia** and **3ib** in 71% and 76% yields, respectively.

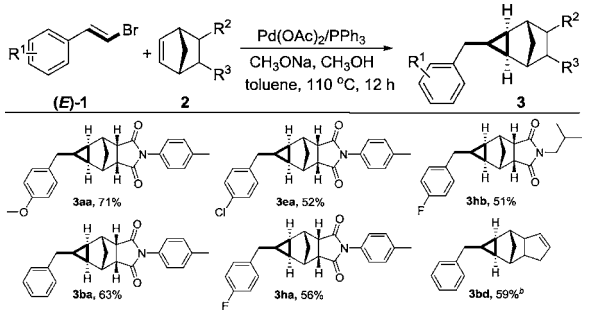
After the scope of the (*Z*)-2-bromovinylarenes was screened, another coupling partner, norbornene derivatives, was investigated. *endo*-*N*-Isobutylnorbornenesuccinimide **2b** was coupled smoothly with (*Z*)-vinyl bromides to give corresponding products **3db**, **3fb**, and **3hb−ib** in good to high yields under the optimized reaction conditions. Norbornene itself **2c** also provided the desired methylcyclopropanes with good yields in the presence of 4.0 equiv of CH_3ONa (Scheme 2, **3ac**, **3cc−dc**, **3hc**). Functionalized norbornene derivatives such as (1*R*,4*S*)-1,4-dihydro-1,4-methanonaphthalene-5,8-diyl diacetate successfully produced the corresponding methylcyclopropanes in good to excellent yields (Scheme 2, **3ad**, **3cd**, **3dd**, **3hd**). Cyclohexene was also employed as alkene to carry out the [2 + 1] cycloaddition reaction, however, the reaction did not proceed smoothly. The structure of products was further confirmed unambiguously by X-ray crystallography of **3da** (see the SI, Figure S1). The formed methylcyclopropane subunit took the *exo*-face of norbornane.

Subsequently, (*E*)-2-bromovinylarene substrates (***E*)-1** were investigated, and the corresponding methylcyclopropane prod-

DOI: 10.1021/acs.orglett.5b01603
Org. Lett. 2015, 17, 3678−3681

ucts **3aa**, **3ba**, **3ea**, **3ha**, **3hb**, and **3bd** were obtained under the same reaction conditions (Scheme 3, 71%, 63%, 52%, 56%, 51%, and 59% yields). Obviously, the (*Z*)-2-bromovinylarene substrates provided better yields than that of (*E*)-ones. It may be that the benzene ring of (*Z*)-2-bromovinylarene stabilizes the norbornenylpalladium intermediate via favorable interaction between the π system of benzene ring and Pd center.[18] However, (*E*)-2-bromovinylarene cannot exert the same stabilizing role because it lacks such space advantage.

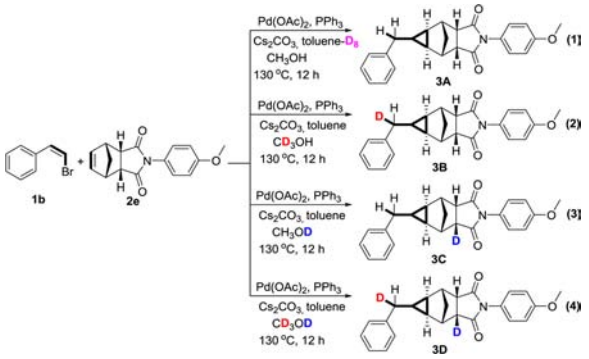
Scheme 3. Substrate Scope of Pd-Catalyzed Methylcyclopropanation of Norbornenes with (*E*)-Vinyl Bromides[a]



[a]Reaction conditions unless otherwise noted: (*E*)-**1** (0.55 mmol), **2** (0.5 mmol), $Pd(OAc)_2$ (0.05 mmol), PPh_3 (0.11 mmol), CH_3ONa (1.5 mmol), toluene (2.0 mL), CH_3OH (0.2 mL), 110 °C, 12 h in sealed tube. Isolated yields are shown. [b]Reaction conditions: **1** (0.5 mmol), **2** (0.6 mmol), $Pd(OAc)_2$ (0.05 mmol), PPh_3 (0.11 mmol), CH_3ONa (2.0 mmol), toluene (2.0 mL), CH_3OH (0.2 mL).

Where did the additional hydrogen atom came from? In order to answer the question, deuterium-labeling experiments were carried out using (*Z*)-(2-bromovinyl)benzene **1b** and *endo*-*N*-(*p*-methoxy)phenylnorbornenesuccinimide **2e** as model substrates (Scheme 4).[19] First, when toluene-d_8 was used as solvent and CH_3OH was employed as additive, nondeuterated methylcyclopropane **3A** was obtained in 73% yield (Scheme 4, eq 1). Second, when CD_3OH was employed as the additive and toluene was used as solvent, benzyl methylene-deuterated methylcyclopropane **3B** was successfully isolated in 55% yield (Scheme 4, eq 2). Subsequently, the reaction was investigated again using CH_3OD as additive and toluene as solvent, methylcyclopropane **3C** of α-deuterium of one carbonyl was obtained in 62% yield (Scheme 4, eq 3). Finally, when the reaction was carried out in toluene using CD_3OD as additive, another methylcyclopropane **3D** with both an α-deuterium of one carbonyl and a methylene-deuterated of benzyl was produced successfully in 45% yield (Scheme 4, eq 4).

Scheme 4. Deuterium-Labeling Studies



The α-H of carbonyl tended to undergo hydrogen/deuterium exchange with CH_3OD or CD_3OD in the presence of base owing to its relatively small pK_a. In order to see whether the H/D exchange is caused by its acidity, deuterium-labeling experiments of the **2e** and **3A** were carried out, respectively, in the absence of $Pd(OAc)_2$ and PPh_3, only using Cs_2CO_3 as base and CH_3OD as additive. However, no product with an α-deuterium of carbonyl was observed. This meant that the H/D exchange of the α-position of carbonyl is not because of its acidity, but the catalytic cycle may have a key influence on the H/D exchange.

On the basis of the current experimental results and related precedents,[13−16,20] a postulated mechanism was proposed (Figure 1). The oxidative addition of palladium(0) species to (*Z*)-bromostyrene derivative **1** produced (*Z*)-styrylpalladium(II) bromide **I**. Subsequently, the *syn* addition of **I** to norbornene **2** at the *exo*-face generated norbornenyl palladium complex **II**. Palladium complexes might exist in an equilibrium between neutral and cationic species.[21] The polar solvent could stabilize the cationic species and the polarity of solvent toluene would be increased in the presence of CD_3OD, thus rendering a cationic palladium species **III** as the major intermediate, which was called the outer form.[22] Subsequently, "bridging" palladium complex **IV** was generated.[23] Thus, the corresponding norbornene fragment became more positively charged to prompt the α-H/D exchange in the presence of base, while CD_3OD coordinated to the Pd(II) and provided a D from OD group. The olefin of the intermediate **VI** coordinated to the Pd center, which was followed by an insertion reaction to produce cyclopropanepalladium intermediate **VII**. The selective β-H elimination of **VII** yielded Pd−D complex **VIII** and released methanal.[24] Reductive elimination of complex **VIII** produced methylcyclopropane derivatives **3** and regenerated Pd(0).

Figure 1. Proposed reaction mechanism for the palladium-catalyzed methylcyclopropanation.

In conclusion, we have developed a novel $Pd(OAc)_2/PPh_3$-catalyzed [2 + 1] cycloaddition domino reaction of vinyl bromides to norbornene derivatives involving a protonation process and an additional H/D exchange from CD_3OD. By this protocol, a methylcyclopropane subunit was installed via the 3-fold domino reaction including Heck-type reaction/C−C bond activation/protonation. Preliminary deuterium-labeling studies demonstrated where the proton came from. This method is unusual, but practical, which complemented the classic methods for the fast synthesis of multiple substituted methylcyclopropane derivatives. Further investigation of the reaction mechanism is underway.

DOI: 10.1021/acs.orglett.5b01603
Org. Lett. 2015, 17, 3678−3681

■ ASSOCIATED CONTENT

Supporting Information

Experimental details, characterization data, full spectroscopic data for all new compounds, and X-ray crystallographic data. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b01603.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: wlbao@zju.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support from the Natural Science Foundation of China (No. 21072168) and the PhD research startup foundation of Jiangxi University of Science and Technology (No. jxxjbs15009) is greatly appreciated.

■ REFERENCES

(1) (a) Crowley, M. P.; Inglis, H. S.; Snarey, M.; Thain, E. M. *Nature* **1961**, *191*, 281. (b) Hata, Y.; Zimmermann, S.; Quitschau, M.; Kaiser, M.; Hamburger, M.; Adams, M. *J. Agric. Food Chem.* **2011**, *59* (17), 9172.

(2) (a) Pietruszka, J. *Chem. Rev.* **2003**, *103*, 1051. (b) Hiratsuka, T.; Suzuki, H.; Kariya, R.; Seo, T.; Minami, A.; Oikawa, H. *Angew. Chem., Int. Ed.* **2014**, *53*, 5423.

(3) (a) Hofmann, K.; Jucker, O.; Miller, W. R.; Young, A. C., Jr.; Tausig, F. *J. Am. Chem. Soc.* **1954**, *76* (7), 1799.

(4) (a) Chen, J.; Levant, B.; Jiang, C.; Keck, T. M.; Newman, A. H.; Wang, S. *J. Med. Chem.* **2014**, *57*, 4962.

(5) (a) Wiberg, K. B. *Acc. Chem. Res.* **1996**, *29*, 229. (b) de Meijere, A. *Chem. Rev.* **2003**, *103*, 931. (c) Fedoryñski, M. *Chem. Rev.* **2003**, *103*, 1099. (d) Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977. (e) Reissig, H.-U.; Zimmer, R. *Chem. Rev.* **2003**, *103*, 1151. (f) Wessjohann, L. A.; Brandt, W.; Thiemann, T. *Chem. Rev.* **2003**, *103*, 1625.

(6) (a) *Carbocyclic Three-Membered Ring Compounds*; de Meijere, A., Ed.; Houben-Weyl, Thieme: Stuttgart, 1997. (b) Brandi, A.; Goti, A. *Chem. Rev.* **1998**, *98*, 589. (c) Rubin, M.; Rubina, M.; Gevorgyan, V. *Chem. Rev.* **2007**, *107*, 3117. (d) Shi, M.; Lu, J.-M.; Wei, Y.; Shao, L.-X. *Acc. Chem. Res.* **2012**, *45*, 641. (e) Zhang, D.-H.; Tang, X.-Y.; Shi, M. *Acc. Chem. Res.* **2014**, *47*, 913.

(7) (a) Goudreau, S. R.; Charette, A. B. *Angew. Chem., Int. Ed.* **2010**, *49*, 486. (b) Oonishi, Y.; Kitano, Y.; Sato, Y. *Angew. Chem., Int. Ed.* **2012**, *51*, 7305. (c) Masutomi, K.; Noguchi, K.; Tanaka, K. *J. Am. Chem. Soc.* **2014**, *136*, 7627. (d) Du, W.; Gu, Q.; Li, Z.; Yang, D. *J. Am. Chem. Soc.* **2015**, *137*, 1130. (e) Satake, A.; Nakata, T. *J. Am. Chem. Soc.* **1998**, *120*, 10391.

(8) (a) Miki, K.; Nishino, F.; Ohe, K.; Uemura, S. *J. Am. Chem. Soc.* **2002**, *124*, 5260. (b) Biswas, A.; De Sarkar, S.; Tebben, L.; Studer, A. *Chem. Commun.* **2012**, *48*, 5190. (c) Lindsay, V. N. G.; Fiset, D.; Gritsch, P. J.; Azzi, S.; Charette, A. B. *J. Am. Chem. Soc.* **2013**, *135*, 1463.

(9) (a) Simmons, H. E.; Smith, R. D. *J. Am. Chem. Soc.* **1958**, *80*, 5323. (b) Beaulieu, L.-P. B.; Schneider, J. F.; Charette, A. B. *J. Am. Chem. Soc.* **2013**, *135*, 7819.

(10) (a) Xie, H.; Zu, L.; Li, H.; Wang, J.; Wang, W. J. *J. Am. Chem. Soc.* **2007**, *129*, 10886. (b) Xuan, Y.; Nie, S.; Dong, L.; Zhang, J.; Yan, M. *Org. Lett.* **2009**, *11*, 1583.

(11) (a) Bruneau, C. *Angew. Chem., Int. Ed.* **2005**, *44*, 2328. (b) Miege, F.; Meyer, C.; Cossy, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 5932.

(12) (a) Miura, T.; Sasaki, T.; Harumashi, T.; Murakami, M. *J. Am. Chem. Soc.* **2006**, *128*, 2516. (b) Bigeault, J.; Giordano, L.; Buono, G. *Angew. Chem., Int. Ed.* **2005**, *44*, 4753.

(13) (a) Mao, J.-G.; Bao, W.-L. *Org. Lett.* **2014**, *16*, 2646. (b) Mao, J.-G.; Zhang, S.-Q.; Shi, B.-F.; Bao, W.-L. *Chem. Commun.* **2014**, *50*, 3692.

(14) (a) Kuwabe, S.; Torraca, K. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 12202. (b) Tseng, N.-W.; Mancuso, J.; Lautens, M. *J. Am. Chem. Soc.* **2006**, *128*, 5338. (c) Dash, P.; Janni, M.; Perunchera-lathan, S. *Eur. J. Org. Chem.* **2012**, *2012*, 4914.

(15) (a) Palucki, M.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 3395. (b) Torraca, K. E.; Kuwabe, S.-I.; Buchwald, S. L. *J. Am. Chem. Soc.* **2000**, *122*, 12907.

(16) (a) Matsukawa, Y.; Mizukado, J.; Quan, H.; Tamura, M.; Sekiya, A. *Angew. Chem., Int. Ed.* **2005**, *44*, 1128. (b) Gellrich, U.; Meißner, A.; Steffani, A.; Kähny, M.; Drexler, H.-J.; Heller, D.; Plattner, D. A.; Breit, B. *J. Am. Chem. Soc.* **2014**, *136*, 1097.

(17) Mao, J.-G.; Bao, W.-L. *Chem. Commun.* **2014**, *50*, 15726.

(18) (a) Beak, P.; Meyers, A. I. *Acc. Chem. Res.* **1986**, *19*, 356. (b) Beak, P.; Basu, A.; Gallagher, D. J.; Park, Y. S.; Thayumanavan, S. *Acc. Chem. Res.* **1996**, *29*, 552. (c) Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461. (d) Fernández, I.; González, J.; López-Ortiz, F. *J. Am. Chem. Soc.* **2004**, *126*, 12551. (e) Herrero-Gómez, E.; Nieto-Oberhuber, C.; López, S.; Benet-Buchholz, J.; Echavarren, A. M. *Angew. Chem., Int. Ed.* **2006**, *45*, 5455.

(19) In order to avoid the influence of H/D exchange of CD_3OD with $-OCH_3$ of CH_3ONa and CH_3OH from the hydrolyzation of CH_3ONa on deuterium-labeling experiments, Cs_2CO_3 was employed as base to carry out the reaction mechanism research.

(20) (a) Martins, A.; Mariampillai, B.; Lautens, M. In *C-H Activation.*; Yu, J.-Q., Shi, Z., Eds.; Springer: New York, 2010; Vol. *292*, pp 1−33 and most pertinent references therein. (b) Shi, F.; Larock, R. C. C−H Activation. In *Topics in Current Chemistry*; Yu, J.-Q., Shi, Z., Eds.; Springer: New York, 2010; Vol. *292*, pp 123−164 and most pertinent references therein. (c) Desai, L. V.; Sanford, M. S. *Angew. Chem., Int. Ed.* **2007**, *46*, 5737. (d) Enthaler, S.; Company, A. *Chem. Soc. Rev.* **2011**, *40*, 4912. (e) Wu, X.; Fors, B. P.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2011**, *50*, 9943. (f) Shen, C.; Xia, H.; Yan, H.; Chen, X.; Ranjit, S.; Tan, D.; Lee, R.; Huang, K.-W.; Zhang, P.; Liu, X. *Chem. Sci.* **2012**, *3*, 2388. (g) Mo, D.-L.; Yuan, T.; Ding, C.-H.; Dai, L.-X.; Hou, X.-L. *J. Org. Chem.* **2013**, *78*, 11470.

(21) (a) Cabri, W.; Candiani, I. *Acc. Chem. Res.* **1995**, *28*, 2. (b) Amatore, C.; Jutand, A.; Meyer, G.; Mottier, L. *Chem. - Eur. J.* **1999**, *5*, 466. (c) Fristrup, P.; Ahlquist, M.; Tanner, D.; Norrby, P.-O. *J. Phys. Chem. A* **2008**, *112*, 12862. (d) Camasso, N. M.; Pérez-Temprano, M. H.; Sanford, M. S. *J. Am. Chem. Soc.* **2014**, *136*, 12771.

(22) (a) Mattheis, C.; Braunstein, P. *J. Organomet. Chem.* **2001**, *621*, 218. (b) Liu, H.; Chen, C.; Wang, L.; Tong, X. *Org. Lett.* **2011**, *13*, 5072. (c) Jiang, X.; Liu, H.; Gu, Z. *Asian J. Org. Chem.* **2012**, *1*, 16.

(23) (a) Roberts, J. D.; Lee, C. C.; Saunders, W. H., Jr *J. Am. Chem. Soc.* **1954**, *76*, 4501. (b) Li, Y.; Liu, X.; Jiang, H.; Liu, B.; Chen, Z.; Zhou, P. *Angew. Chem., Int. Ed.* **2011**, *50*, 6341. (c) Wu, W.; Jiang, H. *Acc. Chem. Res.* **2014**, *47*, 2483.

(24) (a) Torraca, K. E.; Huang, X.; Parrish, C. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *123*, 10770. (b) Guram, A. S.; Bei, X.; Turner, H. W. *Org. Lett.* **2003**, *5*, 2485. (c) Bei, X.; Hagemeyer, A.; Volpe, A.; Saxton, R.; Turner, H.; Guram, A. S. *J. Org. Chem.* **2004**, *69*, 8626. (d) Vorogushin, A. V.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2005**, *127*, 8146.

DOI: 10.1021/acs.orglett.5b01603
Org. Lett. 2015, 17, 3678−3681