Organic LETTERS

Letter

pubs.acs.org/OrgLett

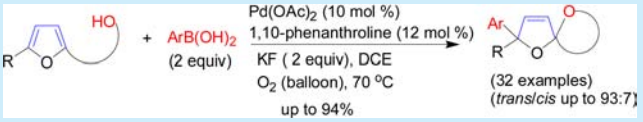
2,5-Oxyarylation of Furans: Synthesis of Spiroacetals via Palladium-Catalyzed Aerobic Oxidative Coupling of Boronic Acids with α-Hydroxyalkylfurans

Jiuyi Li, Hui Peng, Furong Wang, Xiujun Wang, Huanfeng Jiang, and Biaolin Yin*

School of Chemistry and Chemical Engineering, South China University of Technology, Guangzhou 510641, China

Supporting Information

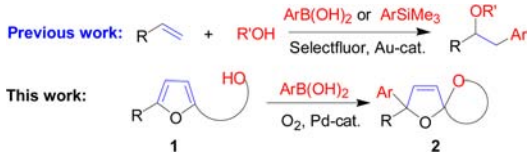
ABSTRACT: A protocol for the 2,5-oxyarylation of furan rings via Pd-catalyzed aerobic oxidative coupling of boronic acids with α-hydroxyalkylfurans is reported. This protocol provides rapid, green access to diverse biologically interesting and synthetically useful unsaturated spiroacetals from sustainable furan derivatives.



Spiroacetals are present in numerous biologically active natural products isolated from plants, fungi, and marine organisms. The spiroacetal moiety contributes to the bioactivities of insect sex pheromones, polyketide antibiotics, and microtubule stabilizing agents, and it represents a privileged scaffold in drug discovery research.[1] Moreover, spiroacetal-containing molecules are useful building blocks for the construction of many biologically active compounds.[2] The documented synthetic approaches to spiroacetals involve dehydration of keto diols,[1b−d] oxa-Michael additions,[3] cycloadditions,[4] palladium(II)- or gold(I)-catalyzed cycloisomerizations involving alkynes as ketone surrogates,[5] and various other methods.[6] Despite great achievements in this area, the development of novel and efficient approaches to this class of compounds from readily available materials is still of great importance.

Because of their low aromaticity, furans can serve as masked alkenes, dienes, enol ethers, and 1,4-diketones,[7] and the furan ring is usually destroyed in reactions that take advantage of this property. In this way, various useful compounds, including spiroacetals, have been synthesized under mild conditions.[8] For example, Vassilikogiannakis et al. reported an elegant route to spiroacetals involving oxidation of a substituted furan nucleus by singlet oxygen.[9] Wu et al. and our group have reported the synthesis of spiroacetals via copper(II)-promoted dehydration of furandiols.[10] Recently, several groups have intensively studied transition-metal-catalyzed oxyarylation of alkenes by vicinal incorporation of an *O*-substituent and an aryl group into a single alkene or diene in one step.[11] Given that the diene moiety of a furan ring is chemically similar to nonaromatic alkenes and dienes, we envisioned that an unprecented dearomatizing oxyarylation of furan rings could be similarly achieved under suitable conditions. Herein, we report that as part of our ongoing work on dearomatizing transformations of sustainably sourced furans and on palladium catalysis,[12] we have developed a palladium-catalyzed the 2,5-oxyarylation of furan rings via aerobic oxidative coupling reaction of boronic acids with α-hydroxyalkylfurans **1** to provide various unsaturated spiroacetals **2** which may be biologically interesting and synthetically useful (Scheme 1).[13]

Scheme 1. Oxyarylation of Nonaromatic Alkenes and Furans

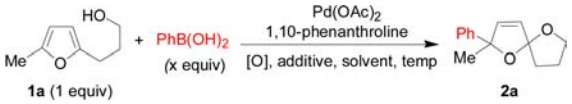


We used the reaction of 3-(5-methylfuran-2-yl)propan-1-ol (**1a**) with phenylboronic acid to optimize the reaction conditions (Table 1). We began by evaluating a series of oxidants with $Pd(OAc)_2$ (5 mol %) as the catalyst and 1,10-phenanthroline (10 mol %) as the ligand at 70 °C in DMF. Strong oxidants such as $K_2S_2O_8$, benzoquinone (BQ), and $PhI(OAc)_2$ were not suitable: complex mixtures were obtained, and none of the desired product (**2a**) was detected (Table 1, entries 1−6). The green oxidant O_2 gave **2a** in 13% yield (Table 1, entry 7) as a mixture of two diastereoisomers (*trans*/*cis* = 52/48) favoring the *trans* isomer; the stereochemistry of the major isomer was determined by means of NOESY experiments on *trans*-**2o** (see the SI). Screening of solvents revealed DCE to be optimal (Table 1, entries 7−11). Various additives were evaluated (Table 1, entries 12−16), and KF was found to increase the yield remarkably (to 73%). When the amounts of $Pd(OAc)_2$ and 1,10-phenanthroline were increased to 10 and 12 mol %, respectively, the yield increased to 93% (Table 1, entry 17). If the amount of phenylboronic acid was increased to 2 equiv, the yield increased even further to 96% (Table 1, entry 18). Elevating or lowering the reaction temperature decreased the yield (Table 1, entries 19 and 20). Thus, we concluded that the optimal conditions for this

Received: May 20, 2016
Published: June 16, 2016

DOI: 10.1021/acs.orglett.6b01472
Org. Lett. 2016, 18, 3226−3229

Table 1. Optimization of Reaction Conditions[a]



entry	[O]	additive	solvent	x	% yield (*trans*/*cis*)[b]
1	$K_2S_2O_8$		DMF	1.5	ND
2	BQ		DMF	1.5	ND
3	$PhI(OAc)_2$		DMF	1.5	ND
4	$Cu(OAC)_2$		DMF	1.5	ND
5	$CuCl_2$		DMF	1.5	ND
6	TEMPO		DMF	1.5	ND
7	O_2		DMF	1.5	13 (52:48)
8	O_2		DCE	1.5	14 (55:45)
9	O_2		toluene	1.5	trace
10	O_2		DXN[c]	1.5	trace
11	O_2		THF	1.5	trace
12	O_2	K_3PO_4	DCE	1.5	49 (68:32)
13	O_2	K_2CO_3	DCE	1.5	59 (58:42)
14	O_2	KF	DCE	1.5	73 (55:45)
15	O_2	*t*-BuOK	DCE	1.5	38 (62:38)
16	O_2	$NHCO_3$	DCE	1.5	70 (52:48)
17[d]	O_2	KF	DCE	1.5	93 (52:48)
18[d]	O_2	KF	DCE	2	96 (55:45)
19[d,e]	O_2	KF	DCE	2	64 (52:48)
20[d,f]	O_2	KF	DCE	2	77 (55:45)

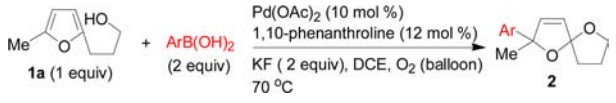
[a]Reaction conditions, unless otherwise noted: **1a** (0.4 mmol), $PhB(OH)_2$ (0.4 mmol), $Pd(OAc)_2$ (5 mol %), 1,10-phenanthroline (10 mol %), additive (2 equiv), [O] (2 equiv or O_2 in a balloon), solvent (2.5 mL), 70 °C, 16 h. [b]Yields and *trans*/*cis* ratios were determined by ^{1}H NMR spectroscopy of the crude products with dibromomethane as an internal standard. The *cis* isomer is the isomer in which the phenyl group is on the same side of dihydrofuran ring as the oxygen group. ND = not detected. [c]DXN = 1,4-dioxane. [d][Pd] = 10 mol %, 1,10-phenanthroline = 12 mol %. [e]Temperature = 80 °C. [f]Temperature = 60 °C.

reaction involved the use of $Pd(OAc)_2$ (10 mol %) as the catalyst, 1,10-phenanthroline (12 mol %) as the ligand, KF (2 equiv) as the additive, DCE as the solvent, and 70 °C as the reaction temperature.

With the optimized reaction conditions in hand, we explored the substrate scope of this transformation (Table 2). Initially, various aryl boronic acids were evaluated. Reactions with phenylboronic acids bearing a H atom, electron-donating substituents (MeO and Me), or moderately electron-withdrawing substituents (F, Cl) proceeded efficiently, providing the desired spiroacetals in moderate to excellent yields (Table 2, entries 1−12), but a strongly electron-withdrawing NO_2 group did not afford the desired product **2n** (Table 2, entry 13). The presence of an *o*- or *m*-Me group on the phenyl ring led to higher diastereoselectivities (Table 2, **2c**−**e**). When Ar was 1-naphthyl with larger steric hindrance, product **2o** was also produced in 52% yield. The use of 2-furanboronic acid resulted in a complex reaction mixture, and **2p** was not isolated (Table 2, entry 15); this result may have been due to the instability of the furan ring under these oxidative conditions.

Next, we investigated the reactions of phenyl boronic acid with various furans **1** to afford spiroacetals (Scheme 2). Substrates with alkyl groups (R = Et, Bn) afforded the expected products in moderate or good yields (**2t** and **2u**). When R was an H atom (**1v**), the yield was very low, possibly owing to the instability of **2v** due to the occurrence of aromatizing

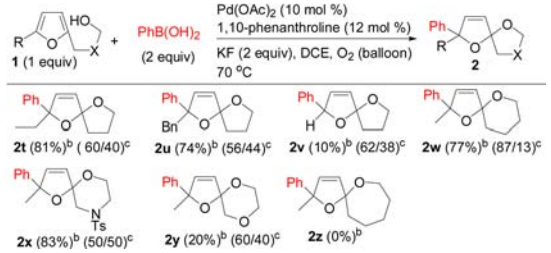
Table 2. Substrate Scope[a]



entry	Ar	**2** (yield[b] (%), *trans*/*cis*[c])
1	Ph	**2a** (83, 61:39)
2	4-Me-Ph	**2b** (73, 60:40)
3	3-Me-Ph	**2c** (63, 71:29)
4	3,5-di-Me-Ph	**2d** (60, 63:37)
5	2,4-di-Me-Ph	**2e** (71, 77:23)
6	2-MeO-Ph	**2f** (41, 58:42)
7	4-MeO-Ph	**2g** (76, 58:42)
8	3-MeO-Ph	**2h** (69, 58:42)
9	3,5-di-MeO-Ph	**2i** (65, 55:45)
10	3-F-Ph	**2j** (64, 57:43)
11	4-Cl-Ph	**2k** (68, 66:34)
12	3-F-4-Me-Ph	**2m** (94, 58:42)
13	4-NO_2-Ph	**2n** (ND)
14	1-Np[d]	**2o** (52, 57:43)
15	2-furyl	**2p** (ND)

[a]**1a** (0.4 mmol). [b]Isolated yield. ND = not detected. The diastereomers of **2a**, **2d**, **2k**, **2m**, and **2x** were separable by silica flash chromatography, and the ratios in parentheses were determined from the isolated weights of the two isomers. [c]Ratios of the other products were determined by ^{1}H NMR spectroscopy of the crude products. [d]1-Np = 1-naphthyl.

Scheme 2. Pd-Catalyzed Coupling of Phenyl Boronic Acid with Various α-Hydroxyalkylfurans[a]



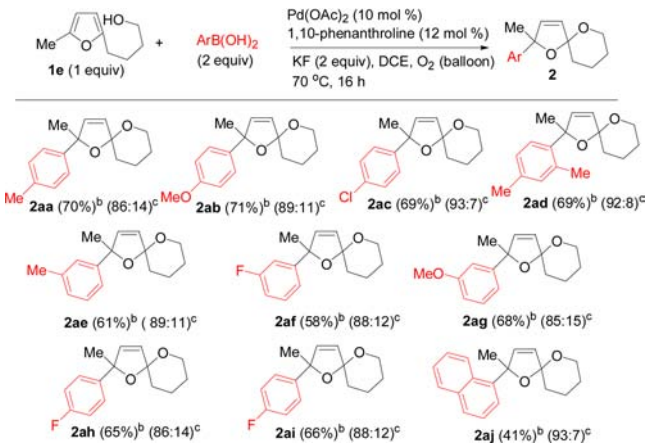
[a]**1**(0.4 mmol). [b]Isolated yields. [c]*Trans*/*cis* ratios established by ^{1}H NMR.

elimination. The structure of the side chain clearly influenced the reaction outcome. When X was $-CH_2CH_2-$, **2w** was formed in 77% yield with high diastereoselectivity for the *trans* isomer. The stereochemistries of the major isomers of the [5.6] spiroacetals were assigned on the basis of NOESY experiments on *trans*-**2ad** and *trans*-**2y** (see the SI). When X was $-N(Ts)CH_2-$ or $-OCH_2-$, the reaction showed little or no diastereoselectivity (**2x** and **2y**). The low yield of **2y** might have resulted from deactivating coordination of the Pd catalyst with the two oxygen atoms tethered in the side chain. A substrate with a six-atom chain did not provide the corresponding [5.7] spiroacetal **2z**.

To further explore the diastereoselectivity of the formation of [5.6] spiroacetals by means of this protocol, we carried out additional reactions of various aryl boronic acids with 4-(5-methylfuran-2-yl)butan-1-ol (**1e**) (Scheme 3). All of the reactions provided the expected products with high diastereoselectivities (dr = 85:15−93:7). The substitutents on the phenyl ring have little influence on the yields and diastereoselectivities of the reaction. Notably, when Ar was 1-

DOI: 10.1021/acs.orglett.6b01472
Org. Lett. 2016, 18, 3226−3229

Scheme 3. Pd-Catalyzed Coupling of 1e with Aryl Boronic Acids[a]

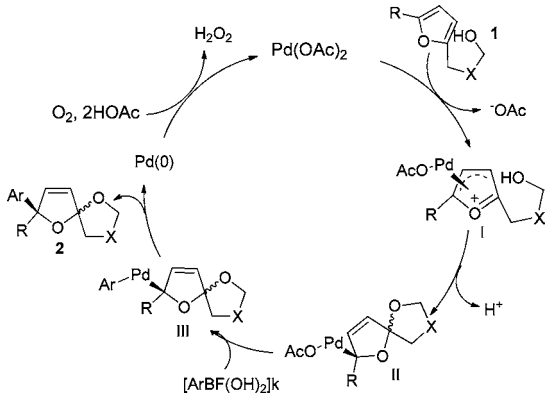


[a]**1e** (0.4 mmol). [b]Isolated yields. [c]*Trans*/*cis* ratios established by ^{1}H NMR.

naphthyl with larger steric hindrance, product **2aj** was produced in a low yield (42%), but with a high diastereoselectivity (93:7).

To explain the reaction outcome, we suggest the following mechanism on the basis of previously reported results on alkene difunctionalization employing boronic acids as the substrates Scheme 4.[14,11] The electrophilic palladation of **1** with

Scheme 4. Proposed Reaction Mechanism

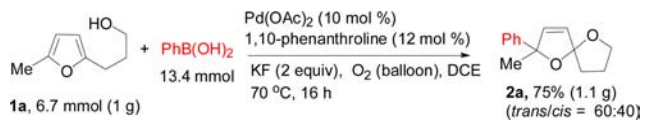


$Pd(OAc)_2$ produces complex **I**. Compound **I** then was acetalized into complex **II**, which was transformed into **2** via transmetalation followed by reduction elimination. The Pd(0) was oxidized into Pd(II) by O_2 to complete the catalytic recycle.

This protocol was readily scalable; when the reaction of **1a** was scaled up to 6.7 mmol (gram scale), spiroacetal **2a** was isolated in 75% yield (Scheme 5).

In summary, we have developed a simple, practical protocol for the synthesis of biologically valuable and synthetically useful unsaturated spiroacetals starting from sustainable furans. This protocol involves palladium-catalyzed oxidative coupling between commercially available boronic acids and α-hydroxyalkylfurans with O_2 as the terminal oxidant and leads to an unprecedented 2,5-oxyarylation of a furan ring. The protocol opens a new avenue for the dearomatizing transformation of furans. Further explorations of the reaction scope, variations of coupling partners, and bioactivities of the obtained products are underway in our laboratory.

Scheme 5. Gram-Scale Reaction of 1a



■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01472.

Experimental procedures; characterization data of new products; ^{1}H and ^{13}C NMR spectra; NOESY spectra of **2o**,**ad**,**y**; HMQC spectrum of **2y** (PDF)

HRMS spectra of all new compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: blyin@scut.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the National Natural Science Foundation of China (21272078 and 21572068) and the Science and Technology Planning Project of Guangdong Province, China (2014A020221035).

■ REFERENCES

(1) For reviews on the bioactivities and syntheses of spiroacetals, see: (a) Kluge, A. F. *Heterocycles* **1986**, *24*, 1699−1740. (b) Fletcher, M. T.; Kitching, W. *Chem. Rev.* **1995**, *95*, 789−828. (c) Perron, F.; Albizati, K. F. *Chem. Rev.* **1989**, *89*, 1617−1661. (d) Aho, J. E.; Pihko, P. M.; Rissa, T. K. *Chem. Rev.* **2005**, *105*, 4406−4440. (e) Jacobs, M. F.; Kitching, W. *Curr. Org. Chem.* **1998**, *2*, 395−436. (f) Mead, K. T.; Brewer, B. N. *Curr. Org. Chem.* **2003**, *7*, 227−256. (g) Booth, Y.; Kitching, W.; De Voss, J. *Nat. Prod. Rep.* **2009**, *26*, 490−525. (h) Cala, L.; Fananas, F. J.; Rodriguez, F. *Org. Biomol. Chem.* **2014**, *12*, 5324−5330. (i) Palmes, J. A.; Aponick, A. *Synthesis* **2012**, *44*, 3699−3721.

(2) For selected examples using spiroacetals as building blocks, see: (a) Wu, B.; Feast, G. C.; Thompson, A. L.; Robertson, J. *J. Org. Chem.* **2012**, *77*, 10623−10630. (b) Aumann, K. M.; Healy, P. C.; Coster, M. J. *Tetrahedron Lett.* **2011**, *52*, 1070−1073. (c) Yin, B.-L.; Wu, Y.-L.; Lai, J.-Q. *Eur. J. Org. Chem.* **2009**, *2009*, 2695−2699. (d) Nikac, M.; Brimble, M. A.; Crumbie, R. L. *Tetrahedron* **2007**, *63*, 5220−5226.

(3) For selected examples, see: (a) Negri, D. P.; Kishi, Y. *Tetrahedron Lett.* **1987**, *28*, 1063−1066. (b) Hao, J.; Forsyth, C. J. *Tetrahedron Lett.* **2002**, *43*, 1−2. (c) Paterson, I.; Coster, M. J.; Chen, D. Y.-K.; Gibson, K. R.; Wallace, D. J. *Org. Biomol. Chem.* **2005**, *3*, 2410−2419. (d) Sosnovskikh, V. Ya.; Korotaev, V.; Yu; Chizhov, D. L.; Kutyashev, I. B.; Yachevskii, D. S.; Kazheva, O. N.; Dyachenko, O. A.; Charushin, V. N. *J. Org. Chem.* **2006**, *71*, 4538−4543. (e) Choi, P. J.; Rathwell, D. C. K.; Brimble, M. A. *Tetrahedron Lett.* **2009**, *50*, 3245−3248.

(4) (a) Tietze, L. F.; Schneider, C. *J. Org. Chem.* **1991**, *56*, 2476−2481. (b) Pale, P.; Bouquant, J.; Chuche, J.; Carrupt, P. A.; Vogel, P. *Tetrahedron* **1994**, *50*, 8035−8052. (c) Lindsey, C. C.; Wu, K. L.; Pettus, T. R. R. *Org. Lett.* **2006**, *8*, 2365−2367. (d) Wu, K.-L.; Wilkinson, S.; Reich, N. O.; Pettus, T. R. R. *Org. Lett.* **2007**, *9*, 5537−5540. (e) Marsini, M. A.; Huang, Y.; Lindsey, C. C.; Wu, K.-L.; Pettus, T. R. R. *Org. Lett.* **2008**, *10*, 1477−1480.

DOI: 10.1021/acs.orglett.6b01472
Org. Lett. 2016, 18, 3226−3229

(5) (a) Li, Y.; Zhou, F.; Forsyth, C. J. *Angew. Chem., Int. Ed.* **2007**, *46*, 279−282. (b) Liu, B.; De Brabander, J. K. *Org. Lett.* **2006**, *8*, 4907−4910. (c) Ravindar, K.; Reddy, M. S.; Lindqvist, L.; Pelletier, J.; Deslongchamps, P. *Org. Lett.* **2010**, *12*, 4420−4423. (d) Li, X.; Chianese, A. R.; Vogel, T.; Crabtree, R. H. *Org. Lett.* **2005**, *7*, 5437−5440. (e) Messerle, B. A.; Vuong, K. Q. *Pure Appl. Chem.* **2006**, *78*, 385−390. (f) Wu, H.; He, Y.-Pi.; Gong, L.-Z. *Org. Lett.* **2013**, *15*, 460−463. (g) Barluenga, J.; Mendoza, A.; Rodriguez, F.; Fananas, F. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 1644−1647.

(6) For selected recent examples of syntheses of spiroacetals, see: (a) Peh, G. R.; Floreancig, P. E. *Org. Lett.* **2015**, *17*, 3750−3753. (b) Fuwa, H.; Sakamoto, K.; Muto, T.; Sasaki, M. *Org. Lett.* **2015**, *17*, 366−369. (c) Han, X.; Floreancig, P. E. *Angew. Chem., Int. Ed.* **2014**, *53*, 11075−11078. (d) Singh, A. A.; Rowley, J. A.; Schwartz, B. D.; Kitching, W.; De Voss, J. J. *J. Org. Chem.* **2014**, *79*, 7799−7821. (e) Butkevich, A. N.; Corbu, A.; Meerpoel, L.; Stansfield, I.; Angibaud, P.; Bonnet, P.; Cossy, J. *Org. Lett.* **2012**, *14*, 4998−5001. (f) Chang, S.; Britton, R. *Org. Lett.* **2012**, *14*, 5844−5847.

(7) (a) Lipshutz, B. H. *Chem. Rev.* **1986**, *86*, 795−819. (b) Bur, S. K.; Padwa, A. *Chem. Rev.* **2004**, *104*, 2401−2432. (c) Lichtenthaler, F. W. *Acc. Chem. Res.* **2002**, *35*, 728−737. (d) Rosatella, A. A.; Simeonov, S. P.; Frade, R. F. M.; Afonso, C. A. M. *Green Chem.* **2011**, *13*, 754−793. (e) Gallezot, P. *Chem. Soc. Rev.* **2012**, *41*, 1538−1558. (f) van Putten, R. J.; van der Waal, J. C.; de Jong, E.; Rasrendra, C. B.; Heeres, H. J.; de Vries, J. G. *Chem. Rev.* **2013**, *113*, 1499−1597. (g) Trushkov, I. V.; Uchuskin, M. G.; Butin, A. V. *Eur. J. Org. Chem.* **2015**, *2015*, 2999−3016.

(8) For selected recent examples, see: (a) Palmer, L. I.; Read de Alaniz, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 7167−7170. (b) Veits, G. K.; Wenz, D. R.; Read de Alaniz, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 9484−9487. (c) Kalaitzakis, D.; Montagnon, T.; Alexopoulou, I.; Vassilikogiannakis, G. *Angew. Chem., Int. Ed.* **2012**, *51*, 8868−8871. (d) Nicolaou, K. C.; Hale, C. R. H.; Ebner, C.; Nilewski, C.; Ahles, C. F.; Rhoades, D. *Angew. Chem., Int. Ed.* **2012**, *51*, 4726−4730. (e) Abaev, V. T.; Plieva, A. T.; Chalikidi, P. N.; Uchuskin, M. G.; Trushkov, I. V.; Butin, A. V. *Org. Lett.* **2014**, *16*, 4150−4153. (f) Kuznetsov, A.; Makarov, A.; Rubtsov, A. E.; Butin, A. V.; Gevorgyan, V. *J. Org. Chem.* **2013**, *78*, 12144−12153.

(9) For reviews, see: (a) Montagnon, T.; Kalaitzakis, D.; Triantafyllakis, M.; Stratakis, M.; Vassilikogiannakis, G. *Chem. Commun.* **2014**, *50*, 15480−15498. (b) Montagnon, T.; Noutsias, D.; Alexopoulou, I.; Tofi, M.; Vassilikogiannakis, G. *Org. Biomol. Chem.* **2011**, *9*, 2031−2039.

(10) (a) Gao, Y.; Wu, W.-L.; Ye, B.; Zhou, R.; Wu, Y.-L. *Tetrahedron Lett.* **1996**, *37*, 893−896. (b) Gao, Y.; Wu, W.-L.; Ye, B.; Zhou, R. *Tetrahedron* **1998**, *54*, 12523−12538. (c) Yin, B.-L.; Lai, J.-Q.; Huang, L.; Zhang, X.-Y.; Ji, F.-H. *Synthesis* **2012**, *44*, 2567−2574.

(11) (a) Ramella, V.; He, Z.; Daniliuc, C. G.; Studer, A. *Org. Lett.* **2015**, *17*, 664−667. (b) Hata, K.; He, Z.; Daniliuc, C. G.; Itami, K.; Studer, A. *Chem. Commun.* **2014**, *50*, 463−465. (c) Ball, L. T.; Lloyd-Jones, G. C.; Russell, C. A. *Chem. - Eur. J.* **2012**, *18*, 2931−2937. (d) Melhado, A. D.; Brenzovich, W. E., Jr.; Lackner, A. D.; Toste, F. D. *J. Am. Chem. Soc.* **2010**, *132*, 8885−8887. (e) Zhang, G.; Cui, L.; Wang, Y.; Zhang, L. *J. Am. Chem. Soc.* **2010**, *132*, 1474−1475. (f) Zhu, S.; Ye, L.; Wu, W.; Jiang, H. *Tetrahedron* **2013**, *69*, 10375−10383.

(12) (a) Yin, B.-L.; Lai, J.-Q.; Zhang, Z.-R.; Jiang, H.-F. *Adv. Synth. Catal.* **2011**, *353*, 1961−1965. (b) Yin, B.; Zeng, G.; Cai, C.; Ji, F.; Huang, L.; Li, Z.; Jiang, H. *Org. Lett.* **2012**, *14*, 616−619. (c) Yin, B.; Cai, C.; Zeng, G.; Zhang, R.; Li, X.; Jiang, H. *Org. Lett.* **2012**, *14*, 1098−1101. (d) Yin, B.; Huang, L.; Wang, X.; Liu, J.; Jiang, H. *Adv. Synth. Catal.* **2013**, *355*, 370−376. (e) Yin, B.; Zhang, X.; Liu, J.; Li, X.; Jiang, H. *Chem. Commun.* **2014**, *50*, 8113−8116. (f) Yin, B.; Zhang, X.; Zhang, X.; Peng, H.; Zhou, W.; Liu, B.; Jiang, H. *Chem. Commun.* **2015**, *51*, 6126−6129. (g) Liu, J.; Zhang, X.; Peng, H.; Jiang, H.; Yin, B. *Adv. Synth. Catal.* **2015**, *357*, 727−731. (h) Ji, F.; Peng, H.; Zhang, X.; Lu, W.; Liu, S.; Jiang, H.; Liu, B.; Yin, B. *J. Org. Chem.* **2015**, *80*, 2092−2102. (i) Yuan, B.; Pan, Y.; Li, Y.; Yin, B.; Jiang, H. *Angew. Chem., Int. Ed.* **2010**, *49*, 4054−4058.

(13) For selected examples of syntheses of unsaturated spiroacetals, see: Yang, H.; Feng, J.; Li, Y.; Tang, Y. *Org. Lett.* **2015**, *17*, 1441−1444. (b) Ravindar, K.; Sridhar Reddy, M.; Deslongchamps, P. *Org. Lett.* **2011**, *13*, 3178−3181. (c) Aponick, A.; Li, C.-Y.; Palmes, J. A. *Org. Lett.* **2009**, *11*, 121−124.

(14) For reviews on alkene difunctionalization, see: (a) Chemler, S. R. *Org. Biomol. Chem.* **2009**, *7*, 3009−3019. (b) McDonald, R. I.; Liu, G.; Stahl, S. S. *Chem. Rev.* **2011**, *111*, 2981−3019.

DOI: 10.1021/acs.orglett.6b01472
Org. Lett. 2016, 18, 3226−3229