Organic LETTERS

Letter

pubs.acs.org/OrgLett

Pyridyl Directed Catalyst-Free *trans*-Hydroboration of Internal Alkynes

Kang Yuan,[†] Naoya Suzuki,[‡] Soren K. Mellerup,[†] Xiang Wang,[†] Shigehiro Yamaguchi,[‡] and Suning Wang*[,†,§]

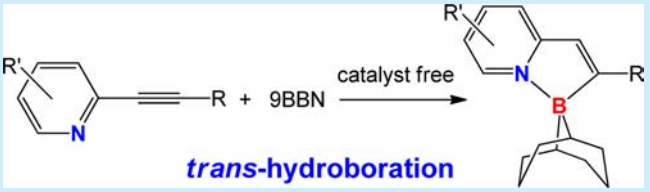
[†]Department of Chemistry, Queen's University, Kingston, Ontario K7L 3N6, Canada

[‡]Department of Chemistry, Graduate School of Science, Nagoya University, Furo, Chikusa, Nagoya 464-8602, Japan

[§]Beijing Key Laboratory of Photoelectronic/Electrophotonic Conversion Materials, School of Chemistry, Beijing Institute of Technology, Beijing 100081, P. R. China

Supporting Information

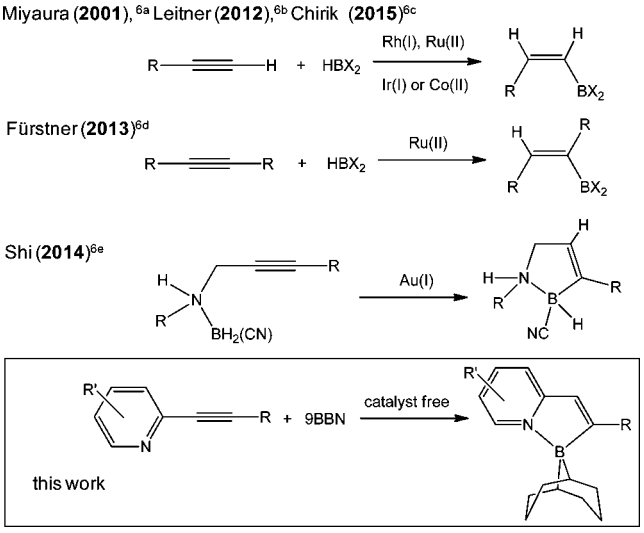
ABSTRACT: We report the first examples of straightforward *trans*-hydroboration of internal alkynes at room temperature with 9-BBN, producing five-membered BN-heterocycles. Contrary to conventional *cis*-hydroboration, we demonstrate that the introduction of a pyridyl group switches the stereoselectivity of the reaction. A hydride migration mechanism has been proposed and supported by DFT calculations for the *trans*-hydroboration. This new hydroboration approach allows facile construction of new blue fluorescent BN-heterocyclic compounds.



Hydroboration, first reported by Hurd and revitalized by Brown and others, represents one of the simplest methods of generating boron containing compounds.[1,2] Hydroboration of alkynes, for instance, is an effective strategy to synthesize vinylborane derivatives, which are useful reagents for the construction of substituted alkenes and boron-containing functional materials.[3,4] Although there remains some controversy with respect to the mechanism of hydroboration, it is generally accepted that the hydroboration of alkynes occurs in a concerted manner via a four-membered transition state formed by the borane and alkyne. Subsequent B−H bond breaking and simultaneous C−H/C−B bond formation ultimately leads to *cis*-addition products as necessitated by the transition state geometry. Alternative hydroboration protocols have been reported by Vedejs, Curran, and Ingleson,[5] where borenium cations were used to hydroborate alkenes and alkynes, although stereoselectivity was not determined for products generated from the latter.

Due to the *cis*-selective nature of traditional hydroboration, obtaining *trans*-hydroboration products remains a synthetic challenge. In fact, great efforts have been devoted to achieving *trans*-hydroboration (Scheme 1).[6] Miyaura and co-workers first reported the use of Ir or Rh catalysts for the *trans*-hydroboration of terminal alkynes.[6a] Ru and Co complexes were also reported as effective terminal alkyne *trans*-hydroboration catalysts.[6b−d] Recently, Fürstner et al. reported a series of Ru catalysts which facilitate hydroboration of internal alkynes in a *trans*-fashion and show good tolerance toward various functional groups as well as good selectivity with most substrates.[6d] Shi et al. demonstrated the use of gold triazole complexes for the synthesis of cyclic aminoboranes via catalytic *trans*-hydroboration.[6e] Donor-directed hydroboration of internal alkynes was investigated previously,[7] where ether, amine, and phosphinites were used to increase the regioselectivity of the reaction; however, no *trans*-hydroboration products were obtained. Despite the success of these catalytic *trans*-hydroboration and donor-directed hydroboration methods, catalyst-free *trans*-hydroboration remains elusive.

Scheme 1. Recent Examples of *trans*-Hydroboration and This Work



Received: December 29, 2015
Published: February 1, 2016

DOI: 10.1021/acs.orglett.5b03698
Org. Lett. 2016, 18, 720−723

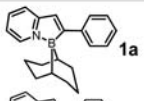
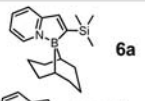
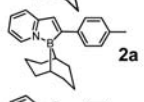
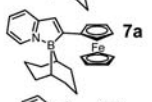
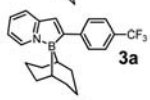
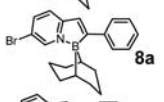
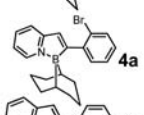
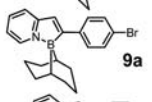
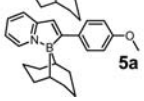
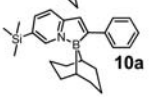
The synthesis of five-membered BN heterocycles has been of longstanding interest due to their interesting photophysical properties and unique reactivities.[8] We have shown that such compounds can display intriguing photochromism, making them promising candidates in optoelectronic devices.[8c−e] Yamaguchi and others have demonstrated that BN embedded π-conjugated systems show intense fluorescence and can act as electron-transporting materials in organic electronic devices.[8f,g] The typical method of introducing the boryl group into the aforementioned systems mainly involves the use of organolithium reagents. Shi and co-workers tried to prepare cyclic aminoborane derivatives with the hydroboration protocol developed by Vedejs,[5a] but were unsuccessful due to either the low reactivity of the alkyne or the occurrence of double hydroboration.[6e]

Herein, we describe the first examples of facile, catalyst-free, *trans*-selective hydroboration of 2-pyridyl alkynes with 9-borabicyclo[3.3.1]nonane (9-BBN) and the utility of this reaction in the construction of new blue fluorescent BN-heterocycles. The pyridyl group was found to function as a directing group and plays a key role in this highly stereo- and regioselective *trans*-hydroboration of internal alkynes.

First, hydroboration of 2-(phenylethynyl)pyridine (entry 1 in Table 1) with 9-BBN (1:1 ratio) in either toluene or benzene at room temperature was examined. This reaction produced a blue fluorescent solution after 12 h. The fluorescent product (**1a**) was isolated by column chromatography as a white solid in good isolated yield (60%). Single-crystal X-ray diffraction analysis established that **1a** is a BN-heterocycle with the proton and boron arranged in a *trans*-manner (Figure 1). The B−N and B−C bonds in **1a** are similar to other N,C-chelated BR_2 compounds that contain bulky R groups such as mesityl.[8] NMR spectra showed that compound **1a** formed in ~90% yield, demonstrating the high stereoselectivity of this reaction. The relatively low isolated yield may be attributed to the fact that compound **1a** slowly degrades under ambient conditions. The *trans*-hydroboration of 2-(phenylethynyl)pyridine is in sharp contrast to the hydroboration of diphenylacetylene with 9-BBN, which was shown to produce the *cis*-addition product.[10] Thus, it was envisioned that the pyridine moiety participates in the *trans*-hydroboration and plays a pivotal role. Next, the scope of this reaction was examined with various substrates containing the requisite 2-alkynylpyridyl group (Table 1). The *trans*-hydroboration was found to be rather general for a variety of substituted 2-(ethynyl)pyridines under mild conditions. For example, substrates that have a weak electron-donating group (entry 2) or a strong electron-withdrawing group on the phenyl ring (entry 3) proceeded in the same manner as 2-(phenylethynyl)pyridine, producing compounds **2a** and **3a**, respectively, in good yields. The *trans*-hydroboration reaction also worked well for bromo-substituted pyridyl or phenyl substrates (entries 4, 8, 9). Replacement of the phenyl group by a bulky TMS group (entry 6) did not retard the reaction, and compound **6a** was obtained, although the reaction is much slower at ambient temperature, compared to entries 1−4 and 7−9. Increasing the reaction temperature to 40 °C for entry 6 greatly accelerated the reaction. Interestingly, the *trans*-hydroboration was also found to tolerate the presence of a ferrocenyl group (entry 7), resulting in the isolation of a ferrocenyl decorated BN-heterocycle **7a**. NMR data indicated that, for most of the substrates investigated, the formation of the BN-heterocycles is essentially quantitative. It is important to note that the *trans*-hydroboration reaction failed for substrates containing a strong electron-donating group on the phenyl ring such as methoxy (entry 5), giving a complex mixture of products which did not include the anticipated BN-heterocycle. In addition, *trans*-hydroboration also failed with electron-rich substituents on the pyridyl ring such as a TMS group at the *meta*-position (entry 10).

In addition to **1a**, the crystal structures of **2a**, **3a**, **6a**, and **7a** were also determined by X-ray diffraction analyses. The structure of **7a** is shown in Figure 2, while other structural data are provided in the Supporting Information. The boron unit in all structures has the

Table 1. Scope of *trans*-Hydroboration of Internal Alkynes[a]

entry	product	yield(%)	entry	product	yield(%)
1	 **1a**	60[b] (90)[c]	6	 **6a**	45 (80)
2	 **2a**	40 (87)	7	 **7a**	75 (90)
3	 **3a**	73 (92)	8	 **8a**	60 (92)
4	 **4a**	70 (93)	9	 **9a**	67 (94)
5	 **5a**	0 (0)	10	 **10a**	0 (0)

[a]All reactions were performed in either toluene or benzene at ambient temperature except for entry 6, which was done at 45 °C. [b]Isolated yield. [c]Yield determined by NMR spectroscopy.

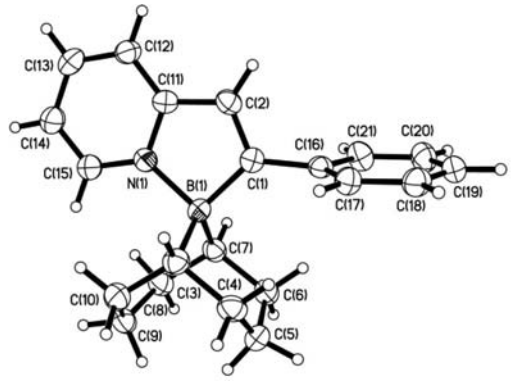


Figure 1. Crystal structure of **1a**.

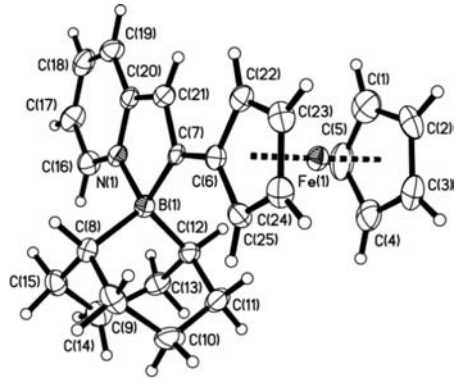


Figure 2. Crystal structure of **7a**.

DOI: 10.1021/acs.orglett.5b03698
Org. Lett. 2016, 18, 720−723

same tetrahedral geometry with similar B−C and B−N bond lengths. The cyclooctyl ring adopts a boat−boat conformation in all structures. One interesting feature of the structures is that for all the phenyl substituted compounds, the phenyl ring is approximately perpendicular to the plane of the BN heterocycle, which is clearly caused by intramolecular steric interactions. In contrast, for the ferrocenyl molecule **7a**, the Cp ring is coplanar with the BN heterocyclic ring, which may be rationalized in terms of decreased interactions of the Cp *ortho*-H atoms with the H atom of the olefinic bond, compared to the phenyl ring.

To gain insights into the unusual *trans*-hydroboration, the ^{1}H and ^{11}B NMR spectra of the reactions with various substrates were monitored. For most of the substrates, the NMR spectral change with time was difficult to interpret as a result of overlapping peaks. The reaction between 2-(ferrocenylethynyl)-pyridine (**7**) and 9-BBN displayed the most diagnostic NMR change, which is illustrated below. Immediately upon mixing the two components in a 1:1 ratio at ambient temperature, a new set of distinct proton peaks emerged (Figure 3) along with a diagnostic four-

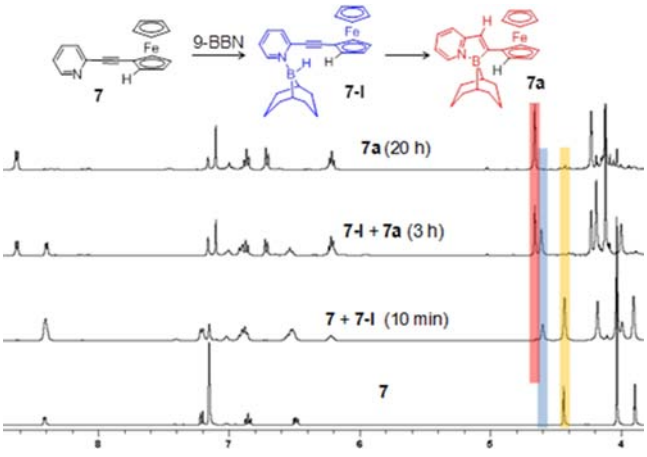


Figure 3. Stacked ^{1}H NMR of the aromatic region showing the stepwise transformation of entry 7 in C_6D_6 under ambient conditions. The diagnostic peaks from the two H atoms of the conjugated Cp ring in **7** (yellow), **7-I** (blue), and **7a** (red) are highlighted.

coordinated ^{11}B peak at 0 ppm (Figure S1), indicating the formation of the borane pyridine adduct **7-I**. After a few hours, a new set of proton peaks appeared along with a new ^{11}B peak at ∼5 ppm corresponding to the final product **7a**. Once ca. 20 h had elapsed, full conversion to the final product was observed. One argument regarding directed hydroboration is whether the borane remains intact upon interaction with the directing groups.[5] Due to inconsistent computational data for a mechanism involving a borenium cation (see Supporting Information) and our NMR data of entry 7, we postulate that the hydroboration occurs via the adduct.

Given that only *cis*-addition would be expected under the traditional hydroboration mechanism, an alternative pathway was proposed and validated by DFT calculations. The calculated reaction pathway for entry 3 is shown in Figure 4. In the proposed mechanism, the mixing of substrate and borane leads to the formation of a Lewis adduct which resides ∼12 kcal/mol lower in energy. Rather than forming a four-membered transition state which would suffer from steric strain, the hydride of the borane migrates to the proximal *sp*-hybridized carbon of the acetylene unit with an activation barrier of 13 kcal/mol. Similar hydride migration was also proposed by Marder and co-workers in an

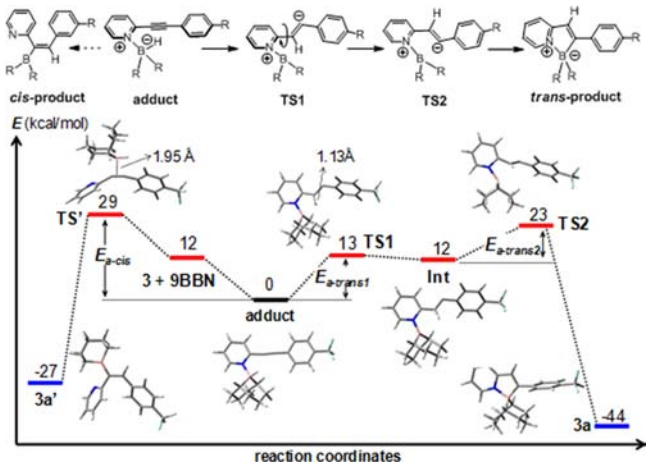


Figure 4. Calculated energy profile at B3LYP/6-31+g(d,p) (cpcm = benzene) comparing the two possible hydroboration pathways for entry 3 (R = CF_3). The electronic energies (kcal/mol) and key structures are shown.

unusual hydroboration of a terminal pyridylalkyne, where the migrating hydride was found to transfer to the distal *sp*-hybridized carbon.[11] Entry 1 was found to display a similar energy profile as entry 3 (see SI).

To rationalize the differing hydride migratory behavior, Mulliken charge population analysis of the Lewis adduct between 2-(phenylethnynyl)pyridine and 9-BBN was performed (Figure S3), and the proximal *sp*-carbon was found to be positively charged, which would encourage hydride migration. The migration results in a zwitterionic intermediate with the distal sp^2-carbon atom possessing a Mulliken charge of −0.864 (see Figure S3). Finally, rotation about the vinylpyridine C−C single bond would then afford the observed products following binding of the negatively charged sp^2-carbon to the now three-coordinated boron. The energy of the second activation barrier, which consists of C−C bond rotation, was found to be slightly smaller than the first at 11 kcal/mol for entry 3 and 10 kcal/mol for entry 1. For comparison, the *cis*-hydroboration pathway was also examined. For entry 3, the overall barrier for *cis*-addition is larger than that of *trans*-addition by 6 kcal/mol when beginning from the resting state (Figure 4) which was determined to be the adduct in solution at room temperature following the combination of substrate and borane. Based on these results, *trans*-hydroboration would be the favored reaction pathway, which agrees with experiment. Detailed mechanistic calculations were also performed on several other substrates (Figures S4−S7) for both *trans*-hydroboration and the pyridyl directed *cis*-hydroboration pathway. In all cases, the energy of all intermediates and transition states for the *trans*-addition are relatively low and less than that of the *cis*-addition, which is in good agreement with the mild conditions employed experimentally. Substituent effects on the calculated structures of the reaction pathways are evident according to the calculated data. While the *cis*-addition pathway remains unaffected by changes in substitution, the energy of both transition states in the *trans*-addition pathway appear to depend on the electronic nature of the substituent. Inductively electron-withdrawing groups such as *p*-CF_3-phenyl stabilize both TS1 and TS2, while electron-donating groups such as *p*-MeO-phenyl destabilize the same two structures as might be expected from their available resonance contributors and the negative charge on the distal sp^2-carbon in the transition states and intermediate (Int). Computational study for an alternative mechanistic

DOI: 10.1021/acs.orglett.5b03698
Org. Lett. 2016, 18, 720−723

pathway involving a borenium cation was also performed for entry 1 (see Figure S8 in SI), which was found to be highly unfavorable energetically compared to the mechanism shown in Figure 4.

The transformation of internal pyridylalkynes to BN-heterocycles via *trans*-hydroboration drastically changes the electronic properties of the molecule, as illustrated by the distinct absorption spectral and color change of **7** (orange) to **7a** (red-orange) (see SI) and the ferrocenyl oxidation potential change from 0.15 V (**7**) to −0.06 V (**7a**, relative to $FeCp_2^+/FeCp_2$). With the exception of compound **7a**, all BN-heterocycles obtained successfully in this work display blue fluorescence in the solid state and solution with λ_{em} = 435 nm (e.g., **1a**, **3a**, **9a**) or 455 nm (e.g., **6a**). The primary absorption band of these compounds is at ∼350 nm, which appears to originate from HOMO → LUMO transitions with $\pi-\pi^*$ character as suggested by TD-DFT calculation data (see Figure S5). Although the quantum efficiencies of these molecules were found to be rather poor in solution, = ∼4% in CH_2Cl_2, a 10-fold increase in luminescent quantum efficiency was observed for BN-heterocycle doped PMMA films (e.g., = ∼40% for **1a** in PMMA) as a result of greatly diminished fluorescence quenching due to the reduced rotation of the substituent groups. These results support that pyridyl-directed *trans*-hydroboration is a viable approach in achieving functional organoboron-based materials.

The unusual *trans*-hydroboration phenomenon appears to be limited to relatively electron-rich boranes such as 9BBN. Preliminary results on hydroboration of pyridylalkynes (e.g., **1**) with other boranes such as $HBMes_2$ indicated that no *trans*-hydroboration product formed. The activation barrier of *trans*-hydroboration with $HBMes_2$ was found to be much greater than that of 9-BBN (see SI). BH_3 was found to form a simple adduct with **1**, and no hydroboration was observed even at elevated temperature (60 °C).

In summary, we have established the catalyst-free *trans*-selective hydroboration of various internal 2-(pyridyl)alkynes with the readily available 9-BBN under mild conditions. The scope of this unprecedented transformation was found to be fairly general toward different substrates. Detailed computational analysis of the proposed mechanism is in excellent agreement with experiment. The new BN-hetereocyclic products obtained via pyridyl-directed hydroboration show interesting photophysical properties. Ongoing efforts are currently being undertaken to extend the scope of this reaction toward creating novel materials with multiple five-membered BN-heterocyclic rings for applications in organic electronics.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b03698.

Synthetic details, NMR spectra, DFT and TD-DFT data, CV diagrams of **7** and **7a**, UV−vis and fluorescence spectra, and X-ray crystallographic data (PDF)

Crystallographic data for **3a**, **7a**, **2a**, **1a**, and **6a** (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: wangs@chem.queensu.ca.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

K.Y., S.M., X.W., and S.W. thank the Natural Sciences and Engineering Research Council of Canada for financial support and the High Performance Computing Virtual Laboratory for computational facilities. N.S. and S.Y. thank JSPS for financial support.

■ REFERENCES

(1) (a) Hurd, D. T. *J. Am. Chem. Soc.* **1948**, *70*, 2053. (b) Brown, H. C.; Rao, B. C. *J. Am. Chem. Soc.* **1956**, *78*, 5694. (c) Brown, H. C. *Hydroboration*; W. A. Benjamin: New York, 1962.

(2) (a) Brown, H. C. *Organic Syntheses via Boranes*; Wiley: New York, 1975. (b) Pelter, A.; Smith, K.; Brown, H. C. *Borane Reagents*; Academic Press: New York, 1988. (c) Hall, D. G., Ed. *Boronic Acids. Preparation, Applications in Organic Synthesis and Medicine*; Wiley-VCH: Weinheim, 2005. (d) Dhillon, R. S. *Hydroboration and Organic Synthesis*; Springer: Germany, 2007.

(3) (a) Beletskaya, I.; Pelter, A. *Tetrahedron* **1997**, *53*, 4957. (b) Trost, B. M.; Ball, Z. T. *Synthesis* **2005**, *2005*, 853. (c) Barbeyron, R.; Benedetti, E.; Cossy, J.; Vasseur, J.; Arseniyadis, S.; Smietana, M. *Tetrahedron* **2014**, *70*, 8431.

(4) (a) Jäkle, F. *Chem. Rev.* **2010**, *110*, 3985. (b) Entwistle, C. D.; Marder, T. B. *Chem. Mater.* **2004**, *16*, 4574. (c) Lorbach, A.; Hübner, A.; Wagner, M. *Dalton Trans.* **2012**, *41*, 6048. (d) Yuan, Z.; Taylor, N. J.; Marder, T. B.; Williams, I. D.; Kurtz, S. K.; Cheng, L.-T. *J. Chem. Soc., Chem. Commun.* **1990**, *21*, 1489. (e) Matsumi, N.; Naka, M. K.; Chujo, Y. *J. Am. Chem. Soc.* **1998**, *120*, 5112. (f) Lorbach, A.; Bolte, M.; Li, H.; Lerner, H.-W.; Holthausen, M. C.; Jäkle, F.; Wagner, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 4584. (g) Guo, F.; Yin, X.; Pammer, F.; Cheng, F.; Fernandez, D.; Lalancette, R. A.; Jäkle, F. *Macromolecules* **2014**, *47*, 7831. (h) Ji, L.; Edkins, R. M.; Sewell, L. J.; Beeby, A.; Batsanov, A. S.; Fucke, K.; Drafz, M.; Howard, J. A. K.; Moutounet, O.; Ibersiene, F.; Boucekkine, A.; Furet, E.; Liu, Z.; Halet, J.-F.; Katan, C.; Marder, T. B. *Chem. - Eur. J.* **2014**, *20*, 13618. (i) Collings, J. C.; Poon, S.-Y.; Le Droumaguet, C.; Charlot, M.; Katan, C.; Palsson, L. O.; Beeby, A.; Mosely, J. A.; Kaiser, H. M.; Kaufmann, D. E.; Wong, W.-Y.; Blanchard-Desce, M.; Marder, T. B. *Chem. - Eur. J.* **2009**, *15*, 198.

(5) (a) Scheideman, M.; Shapland, P.; Vedejs, E. *J. Am. Chem. Soc.* **2003**, *125*, 10502. (b) Pan, X.; Boussonnie, A.; Curran, P. D. *J. Am. Chem. Soc.* **2013**, *135*, 14433. (c) Cade, I. A.; Ingleson, M. J. *Chem. - Eur. J.* **2014**, *20*, 12874.

(6) (a) Ohmura, T.; Yamamoto, Y.; Miyaura, N. *J. Am. Chem. Soc.* **2000**, *122*, 4990. (b) Gunanathan, C.; Hölscher, M.; Pan, F.; Leitner, W. *J. Am. Chem. Soc.* **2012**, *134*, 14349. (c) Obligacion, J. V.; Neely, J. M.; Yazdani, A. N.; Pappas, I.; Chirik, P. J. *J. Am. Chem. Soc.* **2015**, *137*, 5855. (d) Sundararaju, B.; Fürstner, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 14050. (e) Wang, Q.; Motika, S. E.; Akhmedov, N. G.; Petersen, J. L.; Shi, X. *Angew. Chem., Int. Ed.* **2014**, *53*, 5418. (f) Adams, C. J.; Baber, R. A.; Batsanov, A. S.; Bramham, G.; Charmant, J. P. H.; Haddow, M. F.; Howard, J. A. K.; Lam, W. H.; Lin, Z.; Marder, T. B.; Norman, N. C.; Orpen, A. G. *Dalton Trans.* **2006**, 1370.

(7) Deloux, L.; Srebnik, M. *J. Org. Chem.* **1994**, *59*, 6871.

(8) (a) Wakamiya, A.; Yamaguchi, S. *Bull. Chem. Soc. Jpn.* **2015**, *88*, 1357. (b) Yamaguchi, S.; Wakamiya, A. *Pure Appl. Chem.* **2006**, *78*, 1413. (c) Rao, Y.-L.; Amarne, H.; Wang, S. *Coord. Chem. Rev.* **2012**, *256*, 759. (d) Rao, Y.-L.; Wang, S. *Inorg. Chem.* **2011**, *50*, 12263. (e) Rao, Y.-L.; Amarne, H.; Zhao, S.-B.; McCormick, T. M.; Martić, S.; Sun, Y.; Wang, R.-Y.; Wang, S. *J. Am. Chem. Soc.* **2008**, *130*, 12898. (f) Wakamiya, A.; Taniguchi, T.; Yamaguchi, S. *Angew. Chem., Int. Ed.* **2006**, *45*, 3170. (g) Neue, B.; Wakamiya, A.; Fröhlich, R.; Wibbeling, B.; Yamaguchi, S.; Würthwein, E.-U. *J. Org. Chem.* **2013**, *78*, 11747. (h) Ishida, N.; Narumi, M.; Murakami, M. *Org. Lett.* **2008**, *10*, 1279.

(9) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307.

(10) Wang, K. K.; Scouten, C. G.; Brown, H. C. *J. Am. Chem. Soc.* **1982**, *104*, 531.

(11) Entwistle, C. D.; Batsanov, A. S.; Howard, J. A. K.; Fox, M. A.; Marder, T. B. *Chem. Commun.* **2004**, *546*, 702.

DOI: 10.1021/acs.orglett.5b03698
Org. Lett. 2016, 18, 720−723