B,N Heterocycles

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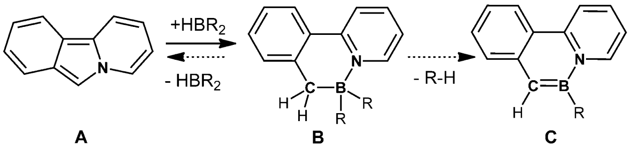
Reversible 1,1-Hydroboration: Boryl Insertion into a C–N Bond and Competitive Elimination of HBR_2 or R–H **

*Deng-Tao Yang, Soren K. Mellerup, Xiang Wang, Jia-Sheng Lu, and Suning Wang**

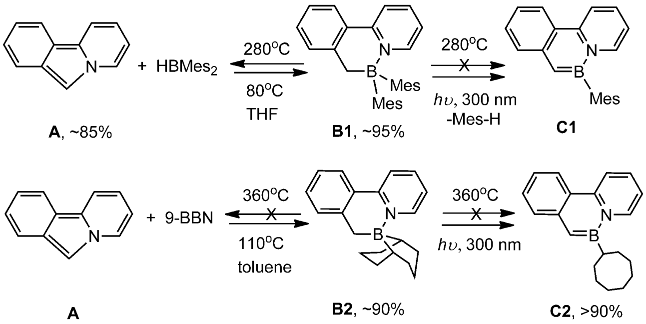
Abstract: *Boranes with the general formula of HBR_2 have been found to undergo a facile 1,1-hydroboration reaction with pyrido[1,2-a]isoindole (**A**), resulting in insertion of a BR_2 unit into a C–N bond and the formation of a variety of BN heterocycles. Investigation on the thermal reactivity of the BN heterocycles revealed that these molecules have two distinct and competitive thermal elimination pathways: HBR_2 elimination (or retro-hydroboration) versus R–H elimination, depending on the R group on the B atom and the chelate backbone. Mechanistic aspects of these highly unusual reactions have been established from both experimental and computational evidence. Adduct formation between HBR_2 and **A** was found to be the key intermediate in 1,1-hydroboration of **A**.*

Organoboron compounds are an important class of molecules, which can be found in a number of important fields[1] including hydrogen storage,[2] optoelectronic devices,[3–4] sensors,[5] and organic synthesis.[6] Of the many organoboron species, boranes (particularly those of the form HBR_2) have long been studied for their use in the functionalization of alkenes and alkynes by 1,2-hydroboration which was originally pioneered by Herbert C. Brown.[7] Despite the large number of examples/uses[8] of 1,2-hydroboration, the related 1,1-hydroboration reactions have, for the most part, eluded researchers. Building upon the seminal work of Wrackmeyer,[9] Erker and co-workers recently reported a 1,1-carboboration[10] involving the simple activation of C–C bonds through the treatment of internal alkynes with several highly electrophilic boranes (e.g. $B(C_6F_5)_3$). This unique reactivity has been extended to the activation/insertion of a BR_2 unit into a C=C bond[11] as well as the formation of borole derivatives,[12] showcasing the potential usefulness of such a chemical transformation. Although a few examples of formal alkyne 1,1-hydroboration involving the use of activating reagents are known,[13] the straightforward 1,1-hydroboration of alkenes or alkynes by common boranes, such as HBR_2, remains unknown. Herein we disclose the first observation of a facile 1,1-hydroboration involving the addition of a variety of HBR_2 into a C–N bond of pyrido[1,2-a]isoindole (Scheme 1, **A**), ultimately generating both known[14] and novel BN heterocycles. Furthermore, during the investigation of the BN heterocyclic compounds **B**, we discovered that depending on the R group of the borane and the ligand backbone in **B**, the 1,1-hydroboration product can either thermally revert back to the borane and **A**, or eliminate an R–H group to form the BN phenanthrene **C**. This unprecedented competing thermal elimination phenomenon is also presented.



Scheme 1. Reversible borane insertion (**A**→**B**) and photo/thermal elimination pathways available to **B**.

Compound **A** was initially obtained from the thermal reaction of **B1**, with the intention of converting it to our reported highly luminescent compound **C1** (Scheme 2)[14] using heat instead of light. Upon heating **B1** in the presence of a small amount of mineral oil at 280 °C for over 1 h, bright green–yellow fluorescent vapors were observed which readily deposited as a green fluorescent solid film at the top of the reaction vessel. This solid was isolated and identified as pyrido[1,2-a]isoindole (or isocarbazole) by ^1H and ^{13}C NMR spectroscopy, mass spectrometry, and X-ray diffraction anal-



Scheme 2. 1,1-Hydroboration of **A** with $HBMes_2$ and 9-BBN, and the thermal and photoreactivity of **B1** and **B2**.

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[*] D.-T. Yang, S. K. Mellerup, X. Wang, Prof. Dr. S. Wang
Department of Chemistry
Queen's University
Kingston, Ontario, K7L 3N6 (Canada)
E-mail: suning.wang@chem.queensu.ca
Dr. J.-S. Lu, Prof. Dr. S. Wang
Beijing Key Laboratory of Photoelectronic/Electrophotonic Conversion Materials, School of Chemistry, Beijing Institute of Technology
5 South Zhongguancun Street, Beijing (P.R. China)

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yses,[15] and can be readily prepared on a gram scale by established procedures.[16] NMR spectroscopic data indicated that compound **A** along with $HBMes_2$ formed quantitatively from the thermal reaction of **B1**, and compound **C1** was not observed at all.[15] Compound **C1** is not an intermediate in the conversion of **B1** into **A** as it remains unchanged when heated to 280 °C in the presence of mesitylene under the same conditions used for the thermal reaction of **B1**. Thus, the transformation of **B1** into **A** could be formally described as a retro-1,1-hydroboration. To obtain mechanistic insights into this highly unusual elimination reaction, we set out to examine the reverse reaction, namely the 1,1-hydroboration of **A** with $HBMes_2$.

Much to our surprise, **A** reacts readily with $HBMes_2$ in THF at 80 °C, generating **B1** in approximately 95 % yield after 3 days (Scheme 2). The fact that 1,1-hydroboration of **A** occurs at a much lower temperature than the reverse retro-hydroboration of **B1** suggests that either the activation barrier from **A** + $HBMes_2$ to **B1** is lower than the retro-1,1-hydroboration of **B1**, or, there is an accessible intermediate from **A** + $HBMes_2$ to **B1**. Although no intermediates were observed in the ^1H NMR spectra tracking the 1,1-hydroboration of **A**, below we will provide evidence which supports that an intermediate is involved in the transformation. The apparent paradox that **A** and $HBMes_2$ can be obtained quantitatively from **B1** at a temperature much higher than the temperature required to form **B1** from **A** + $HBMes_2$ can be explained in that **A** is continuously sublimed from the reaction medium and deposited on the cooler upper surface of the reaction vessel.

To examine the scope of this unprecedented 1,1-hydroboration, the reaction of **A** with the commercially available 9-borabicyclo[3.3.1]nonane (9-BBN) was also studied. After 10 h in toluene at 110 °C, molecule **A** reacts completely with 9-BBN generating a new BN heterocycle **B2** in 90 % yield. Again, no intermediate was detected in the ^1H NMR spectra while monitoring the transformation.[15] The crystal structure of **B2** was determined by X-ray diffraction analysis and is shown in Figure 1. Compound **B2** is a unique member of the BN heterocyclic compounds (Scheme 2) with a chelating cyclooctyl group bound to the boron atom. To examine if the cyclooctyl group prohibits the previously demonstrated photoelimination of related molecules, such as **B1**, the photoreactivity of **B2** was investigated. Upon irradiation with UV light (300 nm) in C_6D_6, **B2** was found to convert into the BN-phenanthrene **C2** quantitatively by an intramolecular R−H elimination process (Scheme 2). Similar to **C1**, molecule **C2** has a low-energy absorption band with well resolved vibrational features at 400–500 nm and is brightly fluorescent with an emission peak at $\lambda_{max} = 520$ nm.[15]

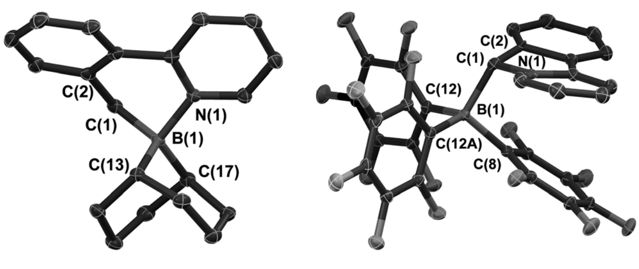


Figure 1. The crystal structures of **B2** (left) and **D4** (right). H atoms are omitted for clarity. Key bond lengths [Å] and angles [°] for **B2**: B(1)–C(1) 1.635(2), B(1)–N(1) 1.651(1), B(1)–C(13) 1.637(2), B(1)–C(17) 1.632(2); C(1)-B(1)-N(1) 100.33(8), C(13)-B(1)-C(17) 104.94(9); for **D4**: B(1)–C(1) 1.718(3), B(1)–C(8) 1.662(3), B(1)–C(12) 1.653(2), C(1)–C(2) 1.506(9), C(1)–N(1) 1.504(7); C(1)-B(1)-C(8) 102.8(2), C(1)-B(1)-C(12) 112.9(1).

Additionally, **A** was found to readily react with highly Lewis acidic boranes, such as $HB(C_6F_5)_2$ and $B(C_6F_5)_3$. As shown by the ^1H NMR spectra in Figure 2, the reaction of **A** with $HB(C_6F_5)_2$ occurred instantaneously at ambient temperature. Rather than forming the BN heterocycle **B3**, a new species **D3** was obtained quantitatively. Based on the NMR spectroscopy data, the structure of **D3** was determined to be an adduct of **A** and $HB(C_6F_5)_2$ as shown in Figure 2. Most significant is the observation that upon heating (80 °C in benzene or 110 °C in toluene), **D3** converts quantitatively into compound **B3**, a new BN heterocycle, which was isolated in 98 % yield and fully characterized by X-ray diffraction analysis.[15] Formally, the conversion of **D3** into **B3** may be described as hydride migration and boryl insertion into a C−N bond. This establishes that the adduct **D3** is a key intermediate involved in the 1,1-hydroboration of **A** with $HB(C_6F_5)_2$. From this result, we expect that the analogous adducts of **A** with $HBMes_2$ and 9-BBN are likely to be involved in the conversion into **B1** and **B2**, respectively.

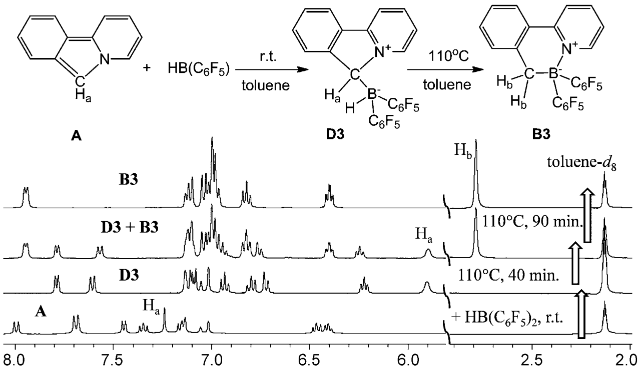
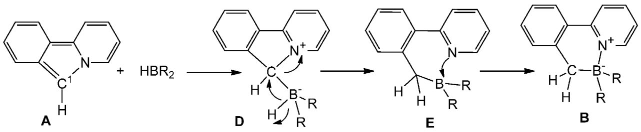


Figure 2. Bottom: The ^1H NMR spectra showing the clean formation of **D3** upon the mixing of **A** and $HB(C_6F_5)_2$ in [D$_8$]toluene at ambient temperature, and the subsequent clean transformation of **D3** to **B3** upon heating at 110 °C. Top: Scheme showing the structure of intermediate **D3** and its conversion into **B3**.

Not surprisingly, the reaction of **A** with $B(C_6F_5)_3$ proceeded in the same manner as that of $HB(C_6F_5)_2$, forming the air-sensitive and colorless adduct **D4** quantitatively. As shown in Figure 1, **D4** possesses a crystallographically imposed mirror plane. Consequently, the C(2) and N(1) atoms in **D4** are disordered. The B(1)−C(1) bond (1.718(3) Å) is quite long, owing to steric congestion around the B atom. The ph-py unit in **D4** has π-stacking interactions with a C_6F_5 ring (C(8) ring) as indicated by some of the short distances (2.92–3.21 Å). The structures of **D3** and **D4** establish that pyrido-[1,2-a]isoindole is a good nucleophile, capable of binding to a trivalent boron center through its C(1) atom. Heating the solution of **D4** in THF or toluene causes the solution color change to deep blue, accompanied by a complex NMR spectral change which is being resolved and will be reported in due course. For less Lewis acidic and sterically encumbered boranes, such as BPh_3, no reaction was observed with **A**.

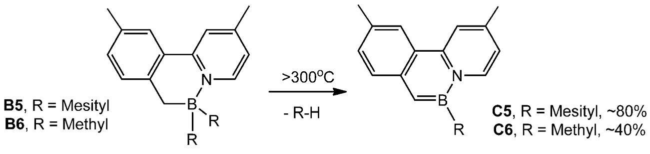
The above examples establish that the 1,1-hydroboration of **A** is a general phenomenon for HBR_2 boranes. Synthetically this is a very useful and convenient reaction for the synthesis of BN-heterocyclic compounds which are either difficult or not possible to obtain by other methods.[14]

Having established that the species **D** is a key intermediate, the transformation of **A** + HBR_2 to **B** is proposed to involve the following sequence (Scheme 3): 1) formation of the four-coordinated borane adduct **D**, 2) a hydride transfer from the boron atom to the carbon atom and cleavage of the C–N bond in **D** resulting in the formation of intermediate **E**, which is likely facilitated by the negatively charged borane and the positively charged nitrogen in **D**, 3) coordination of the nitrogen atom to the electron-deficient boron atom in **E**, forming the chelate product **B**. Mechanistically, the 1,1-hydroboration of **A** with HBR_2 described bears some resemblance to the 1,1-carboboration of an aminohydropentalene derivative with $B(C_6F_5)_2R$ reported by Erker and co-workers.[10] The fact that the borane adduct of **A** with $HBMes_2$ or 9-BBN was not observed at ambient temperature could be explained by the low Lewis acidity of $HBMes_2$ and 9-BBN that prevents adduct formation at ambient temperature. At elevated temperatures, the corresponding adducts could form, but they would be short-lived and undergo a rapid hydride transfer because of the low Lewis acidity of the boron center.



Scheme 3. The proposed mechanism of the 1,1-hydroboration reaction.

To determine if the reversible 1,1-hydroboration is general for other BN heterocycles, we investigated the thermal reaction of the **B2**, **B3**, **B5**, and **B6** (Scheme 4) under the same conditions as **B1**. Molecules **B2** and **B3** do not undergo any chemical change below 360 °C, while above 360 °C they decompose producing unidentifiable species. Oddly enough, heating **B5** and **B6** at 310 °C and 360 °C, respectively, did not result in retro-hydroboration, but instead produced the BN-phenanthrene products **C5** and **C6**, respectively (Scheme 4).[15] Based on these observations it is evident that there are two competing thermal elimination pathways for the BN heterocycles, namely, R–H or HBR_2 elimination, where the substituent groups on ph-py and boron clearly dictate which is preferred.



Scheme 4. The thermal elimination of previously reported **B5** and **B6**.

To explain the two distinct thermal elimination pathways of the BN heterocycles, computational studies using DFT methods were carried out. Prior to modeling the reaction pathways, the nucleophilic nature of **A**'s C(1) atom was confirmed by Mulliken population analysis where it was found to be negatively charged and contributing significantly to the HOMO level.[15] The thermal reaction pathways of **B1** are depicted in Figure 3, while those of the other BN heterocycles can be found in the Supporting Information. The calculated mechanistic pathway is consistent with our proposed mechanism (Scheme 3), in which the calculated activation energy for HBR_2 elimination (E_{a1}) is approximately 100 kJ mol^{-1} less than the R–H elimination barrier (E_{a2}, Figure 3). Not only does this suggest that HBR_2 elimination is favored for **B1**, but it also helps explain why the 1,1-hydroboration of **A** with $HBMes_2$ requires less energy to proceed than the reverse, as the intermediate **D1** resides close in energy and geometry to the transition-state structure **E1***. That this intermediate is not observed experimentally is not surprising given the proximity of the **D1** and **E1*** energy levels. It is interesting to note that there is a large difference between the two product energies of each thermal elimination pathway, where the R–H elimination pathway produces the thermodynamically favored product. As argued before, we suspect that sublimation of **A** away from the reaction mixture as it forms allows for isolation of this kinetic product. Although we attempted to locate the transition states between **A** + $HBMes_2$→**D1** and **B1**→**E1**, they could not be found most likely because they reside very close in energy to the product of each transformation.

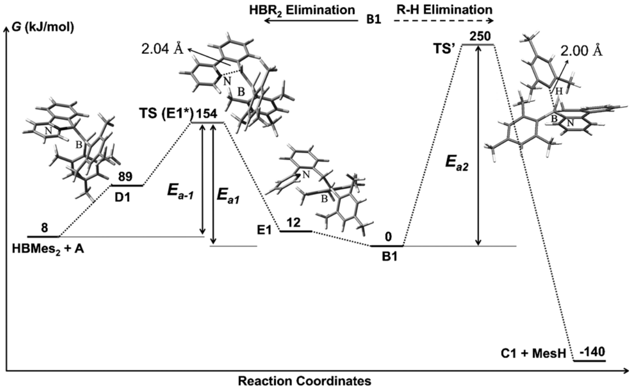


Figure 3. Relative ground-state Gibbs free energies and structures (B3LYP/6-31g*) of the reactant, intermediates, transition states, and products involved in the two thermal elimination pathways of **B1**.

Based on the calculated pathway data of each **B** species (Table 1), different reactivities would be expected based on the R groups at boron and ph-py. In all the other systems, the calculated relative energies of the HBR_2 + **A** (or **A′**, 2,9-dimethylpyrido-[1,2-a]isoindole) molecules were found to be significantly higher than that of $HBMes_2$ + **A**. In the case of **B5** and **B6**, this is most likely the reason that the HBR_2 elimination of **B5** and **B6** is not observed as the products are

Table 1: Summary of activation barriers and pertinent ground-state energies (kJ mol^{-1}) relative to the calculated energies of **B1**–**B6**.

Cmpd	A(A′) + HBR$_2$	E_{a1}	E_{a-1}	E_{a2}	D	C + RH
B1	8	154	146	250	89	−140
B2	95	205	110	287	137	1
B3	139	206	107	277	99	7
B5	54	154	100	256	92	−142
B6	118	227	109	288	145	−29

thermodynamically unstable. It is important to note that **A′** has not been synthesized to date, which further supports this claim. Given that these reactions were carried out at elevated temperatures, the excess kinetic energy of the system could allow the E_{a2} barrier to be crossed for **B5** and **B6**, leading the reaction to the "thermodynamic minimum" that is the R−H elimination products. With respect to **B2** and **B3**, the predicted E_{a-1} barrier is approximately 40 kJ mol^{-1} less than that for **B1**, which correlates nicely with the varying reaction times/temperatures of these three hydroboration reactions. In both cases, neither competing elimination pathway results in the formation of a thermodynamically stable product, which is most likely why heating of **B2** and **B3** does not induce either of these reactivities. Lastly, it is interesting to note that the NMR spectroscopic observation of **D3** is also in agreement with the calculation results, as the adduct **D3** was found to be more thermodynamically stable than the mixture of **A** and HB(C_6F_5)$_2$.[15] Subsequent heating of **D3** gives the reaction mixture enough energy to traverse the activation barrier E_{a-1}, ultimately yielding **B3**.

In summary, the unusual 1,1-hydroboration reaction involving different boranes and molecule **A** has been established, which provides an efficient synthetic method for a variety of BN heterocyclic compounds. It is conceivable that this reactivity could be extended to systems that have similar structural features to those of **A**, and which we are now beginning to examine as a route to new BN heterocycles. Two competitive thermal elimination pathways of BN heterocyclic compounds have been established, one of which could be used for the bulk synthesis of certain BN-phenanthrene compounds through a convenient thermal elimination reaction. Compound **B2** was found to undergo an intramolecular R−H photoelimination, converting the 1,5-cyclooctyl into a 1-cyclooctyl ligand and generating a new BN-phenanthrene **C2**. Mechanistic insight on 1,1-hydroboration of **A** and the two competing thermal elimination pathways of **B** was obtained from experimental work and computational studies.

Keywords: 1,1-hydroboration · BN heterocycles · boryl insertion · thermal elimination

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[1] *Boron Science New Technologies and Applications* (Ed.: N. S. Hosmane), CRC, Taylor & Francis, Boca Raton, **2012**.

[2] a) W. Luo, P. G. Campbell, L. N. Zakharov, S.-Y. Liu, *J. Am. Chem. Soc.* **2011**, *133*, 19326–19329; b) C. W. Hamilton, R. T. Baker, A. Staubitz, I. Manners, *Chem. Soc. Rev.* **2009**, *38*, 279–293.

[3] a) C. D. Entwistle, T. B. Marder, *Angew. Chem. Int. Ed.* **2002**, *41*, 2927–2931; *Angew. Chem.* **2002**, *114*, 3051–3056; b) C. D. Entwistle, T. B. Marder, *Chem. Mater.* **2004**, *16*, 4574–4585; c) A. Wakamiya, T. Taniguchi, S. Yamaguchi, *Angew. Chem. Int. Ed.* **2006**, *45*, 3170–3173; *Angew. Chem.* **2006**, *118*, 3242–3245; d) P. Chen, R. A. Lalancette, F. Jäkle, *Angew. Chem. Int. Ed.* **2012**, *51*, 7994–7998; *Angew. Chem.* **2012**, *124*, 8118–8122; e) A. Lorbach, A. Hübner, M. Wagner, *Dalton Trans.* **2012**, *41*, 6048–6063.

[4] a) Y.-L. Rao, H. Amarne, S.-B. Zhao, T. M. McCormick, S. Martić, Y. Sun, R.-Y. Wang, S. Wang, *J. Am. Chem. Soc.* **2008**, *130*, 12898–12900; b) K. Nagura, S. Saito, R. Fröhlich, F. Glorius, S. Yamaguchi, *Angew. Chem. Int. Ed.* **2012**, *51*, 7762–7766; *Angew. Chem.* **2012**, *124*, 7882–7886; c) Y.-L. Rao, H. Amarne, S. Wang, *Coord. Chem. Rev.* **2012**, *256*, 759–770.

[5] C. R. Wade, A. E. J. Broomsgrove, S. Aldridge, F. P. Gabbäi, *Chem. Rev.* **2010**, *110*, 3958–3984.

[6] a) H. C. Brown, *Tetrahedron* **1961**, *12*, 117–138; b) R. M. Mikhailov, *Organoboron Compounds in Organic Synthesis*, Harwood Academic, **1984**; c) H. C. Brown, *Boranes in Organic Chemistry*, Cornell University Press, Ithaca, **1972**.

[7] a) H. C. Brown, *Hydroboration*, W. A. Benjamin, New York, **1962**; b) H. C. Brown, C. F. Lane, *J. Am. Chem. Soc.* **1970**, *92*, 6660–6661; c) J. V. B. Kanth, H. C. Brown, *J. Org. Chem.* **2001**, *66*, 5359–5365.

[8] a) M. Scheideman, G. Wang, E. Vedejs, *J. Am. Chem. Soc.* **2008**, *130*, 8669–8676; b) H. Braunschweig, R. D. Dewhurst, C. Hörl, A. K. Phukan, F. Pinzner, S. Ullrich, *Angew. Chem. Int. Ed.* **2014**, *53*, 3241–3244; *Angew. Chem.* **2014**, *126*, 3305–3308; c) H. Braunschweig, C. Hörl, *Chem. Commun.* **2014**, *50*, 10983–10985; d) C. D. Entwistle, A. S. Batsanov, J. A. Howard, M. A. Fox, T. B. Marder, *Chem. Commun.* **2004**, 702–703.

[9] a) B. Wrackmeyer, *Coord. Chem. Rev.* **1995**, *145*, 125–156, and references therein; b) B. Wrackmeyer, *Heteroat. Chem.* **2006**, *17*, 188–208, and references therein.

[10] C. Chen, G. Kehr, R. Fröhlich, G. Erker, *J. Am. Chem. Soc.* **2010**, *132*, 13594–13595.

[11] B. H. Xu, G. Kehr, R. Fröhlich, S. Grimme, G. Erker, *J. Am. Chem. Soc.* **2011**, *133*, 3480–3491.

[12] F. Ge, G. Kehr, C. G. Daniliuc, G. Erker, *J. Am. Chem. Soc.* **2014**, *136*, 68–71.

[13] a) J. Ugolotti, G. Dierker, G. Kehr, R. Fröhlich, S. Grimme, G. Erker, *Angew. Chem. Int. Ed.* **2008**, *47*, 2622–2625; *Angew. Chem.* **2008**, *120*, 2662–2665; b) A. Boussonnière, X. Pan, S. J. Geib, D. P. Curran, *Organometallics* **2013**, *32*, 7445–7450.

[14] J.-S. Lu, S. B. Ko, N. R. Walters, Y. Kang, F. Sauriol, S. Wang, *Angew. Chem. Int. Ed.* **2013**, *52*, 4544–4548; *Angew. Chem.* **2013**, *125*, 4642–4646.

[15] See Supporting Information for details.

[16] S. Kajigaeshi, S. Mori, S. Fujisaki, S. Kanemasa, *Bull. Chem. Soc. Jpn.* **1985**, *58*, 3547–3551.

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