

## Heterocycles

Deutsche Ausgabe: DOI: 10.1002/ange.201606177  
Internationale Ausgabe: DOI: 10.1002/anie.201606177

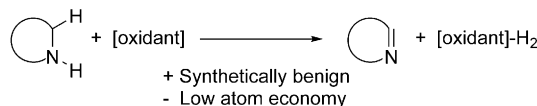
## Tris(pentafluorophenyl)borane-Catalyzed Acceptorless Dehydrogenation of N-Heterocycles

Masahiro Kojima and Motomu Kanai\*

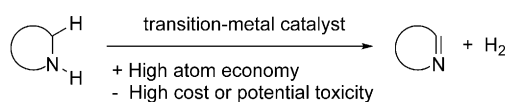
**Abstract:** Catalytic acceptorless dehydrogenation is an environmentally benign way to desaturate organic compounds. This process is traditionally accomplished with transition-metal-based catalysts. Herein, a borane-catalyzed, metal-free acceptorless dehydrogenation of saturated N-heterocycles is disclosed. Tris(pentafluorophenyl)borane was identified as a versatile catalyst, which afforded several synthetically important N-heteroarenes in up to quantitative yield. Specifically, the present metal-free catalytic system exhibited a uniquely high tolerance toward sulfur functionalities, and demonstrated superior reactivity in the synthesis of benzothiazoles compared to conventional metal-catalyzed systems. This protocol can thus be regarded as the first example of metal-free acceptorless dehydrogenation in synthetic organic chemistry.

Nitrogen-containing heteroarenes are a commonly encountered structural motif in pharmaceuticals, natural products, and synthetic materials. Therefore, the development of efficient methods for the synthesis of this compound class is a central research area in synthetic organic chemistry. One method to access these heteroarenes is the dehydrogenation of the corresponding saturated N-heterocycles using a stoichiometric oxidant (Scheme 1 a).<sup>[1]</sup> Conversely, catalytic acceptorless dehydrogenations are more atom efficient<sup>[2]</sup> since no external reagent is required, and in addition, valuable molecular hydrogen is expelled during the desaturation.<sup>[3]</sup> Synthetically, the most relevant reaction conditions have been accomplished with ruthenium-<sup>[4]</sup> or iridium-based<sup>[5]</sup> homogeneous transition-metal catalysts (Scheme 1 b). Fujita, Yamaguchi, et al. have made primary contributions to this field, and reported the catalytic dehydrogenation of 1,2,3,4-tetrahydroquinoline and other cyclic amines using homogeneous iridium catalysts.<sup>[5a,c]</sup> Xiao and co-workers were able to achieve acceptorless dehydrogenations under milder reaction conditions by using cyclometalated iridium complexes, and also disclosed the unique characteristics of using trifluoroethanol as a solvent.<sup>[5b,g]</sup> Crabtree and co-workers used homogeneous iridium/N-heterocyclic carbenes and chelated

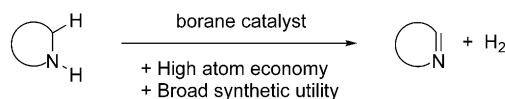
a) Stoichiometric dehydrogenation



b) Metal-catalyzed acceptorless dehydrogenation



c) This work: borane-catalyzed acceptorless dehydrogenation



**Scheme 1.** Dehydrogenation methods for the synthesis of N-heteroarenes.

iridium catalysts for the dehydrogenation of 1,2,3,4-tetrahydroquinoline.<sup>[5c]</sup> Recently, Jones reported related dehydrogenation reactions based on homogeneous iron<sup>[5d]</sup> and cobalt<sup>[5f]</sup> catalysts. These precedents prompted us to explore a new class of acceptorless dehydrogenations, which may be suitable for the synthesis of N-heterocycles with high functional-group tolerance and environmental friendliness.

In an attempt to develop a versatile acceptorless dehydrogenation for the synthesis of N-heteroarenes, we focused our attention on Lewis-acidic borane catalysts in the context of frustrated Lewis pairs (FLPs).<sup>[6]</sup> Borane catalysts play a fundamental role in FLP-mediated hydrogenations,<sup>[7]</sup> but their use in catalytic dehydrogenations of organic compounds has remained unexplored.<sup>[8]</sup> We hypothesized that hydride abstraction from amines by tris(pentafluorophenyl)borane to generate borohydride species,<sup>[9]</sup> and subsequent hydrogen gas evolution through protonolysis of the borohydride, would allow the development of a novel catalytic acceptorless dehydrogenation process. Indeed, catalytic hydride abstraction from an amine and cyclohexadienyl silanes by the electrophilic borane was previously described in transfer hydrogenation<sup>[9b]</sup> and transfer hydrosilylation,<sup>[9f,g,h]</sup> respectively. In addition, the modest coordination ability of the nitrogen lone pair in various N-heteroarenes, together with appropriate sterics on the Lewis acid catalyst, should provide high catalytic turnover numbers. Considering the uniquely high chemoselectivity of borane catalysis and the fact that these systems do not require expensive or toxic metals, borane-catalyzed dehydrogenations should constitute a highly valuable method for the synthesis of N-heteroarenes (Scheme 1 c).

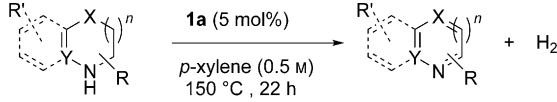
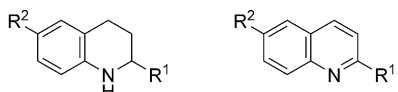
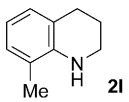
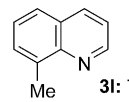
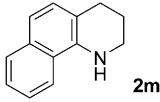
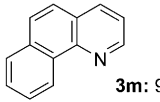
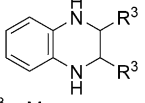
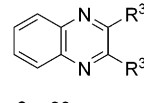
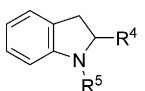
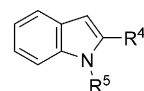
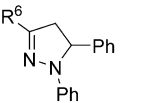
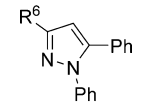
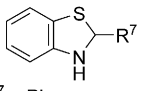
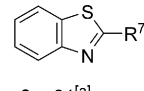
[\*] M. Kojima, Prof. Dr. M. Kanai  
Graduate School of Pharmaceutical Sciences, The University of Tokyo  
Hongo, Bunkyo-ku, Tokyo 113-0033 (Japan)  
E-mail: kanai@mol.f.u-tokyo.ac.jp  
Homepage: [http://www.f.u-tokyo.ac.jp/~kanai/e\\_index.html](http://www.f.u-tokyo.ac.jp/~kanai/e_index.html)  
Prof. Dr. M. Kanai  
Japan Science and Technology Agency, ERATO  
Kanai Life Science Catalysis Project  
Hongo, Bunkyo-ku, Tokyo 113-0033 (Japan)

Supporting information for this article can be found under:  
<http://dx.doi.org/10.1002/anie.201606177>.

Our initial investigations proved the validity of our hypothesis. The catalytic dehydrogenation of 2-methyl-1,2,3,4-tetrahydroquinoline (**2a**) proceeded in the presence of 5 mol % tris(pentafluorophenyl)borane (**1a**) to afford 2-methylquinoline (**3a**) in 92 % yield (Table 1, entry 1).<sup>[10]</sup> In addition, the release of H<sub>2</sub> from **2a** during the dehydrogenation was unambiguously confirmed by a dual reactions experiment.<sup>[11]</sup> Under the optimized reaction conditions, we proceeded to investigate the substrate scope of this catalytic dehydrogenation of N-heterocycles (Table 1). Variation of the substituents at the 2-position of 1,2,3,4-tetrahydroquinoline induced minor effects on the catalytic performance: bulkier alkyl (e.g. butyl; entry 2) or aryl (entries 3–5) substituents did not affect the reaction efficiency negatively. It is noteworthy that the present protocol is tolerant to a Lewis-basic thioether group (entry 6), which is sensitive under the standard oxidation conditions. Tetrahydroquinolines with electron-donating (entries 7 and 8) or electron-withdrawing (entries 9–11) substituents afforded the dehydrogenated products in good to excellent yields. These results suggest that the catalytic efficiency does not depend on the electron density of starting amines. The relatively low yield of 6-methoxytetrahydroquinoline (**2h**) might be due to a potential deactivation of the borane catalyst upon coordination with the oxygen atom of the ether moiety. Under similar reaction conditions, 8-substituted 1,2,3,4-tetrahydroquinolines could also be successfully dehydrogenated (entries 12 and 13). These results demonstrate both the high reactivity and functional-group tolerance of the present dehydrogenation protocol.

Encouraged by these results, we attempted to apply this dehydrogenation to other partially saturated N-heterocycles. Quinoxaline derivatives represent a recurring structural motif in antibiotics such as echinomycin.<sup>[12]</sup> The synthesis of quinoxalines by dehydrogenation would provide a new, practical, and efficient route to this class of N-heteroarenes. Under the optimized reaction conditions, the 1,2,3,4-tetrahydroquinoxaline derivatives **2n** and **2o** were dehydrogenated in good to excellent yield (Table 1, entries 14 and 15), and the difference in steric hindrance at the 2- and 3-positions did not result in a substantial difference with respect to catalytic efficiency. Indoles represent another frequently encountered structural motif in both pharmaceuticals and natural products. Given that the preparation of indoles is well established,<sup>[13]</sup> their dehydrogenation should constitute an attractive synthetic route to indoles. While unsubstituted indoline (**2p**) was dehydrogenated in only modest yield (entry 16) by the present protocol, the dehydrogenation of 2-methylindoline (**2q**) was accomplished in excellent yield (entry 17). It is noteworthy that the dehydrogenation of *N*-methyl indoline (**2r**) also proceeded smoothly (entry 18), because this substrate cannot be efficiently dehydrogenated using transition metal-free aerobic conditions.<sup>[14]</sup> Pyrazoles are another important class of N-heteroarenes with interesting bioactivity, and are present in pharmaceuticals such as celecoxib.<sup>[14]</sup> As pyrazolines can be readily synthesized from hydrazine and enones, their metal-free dehydrogenation would provide direct access to biologically active pyrazoles. Indeed, dehydrogenation of **2s** and **2t** afforded the pyrazoles **3s** and **3t**,

**Table 1:** Substrate generality in the dehydrogenation of the N-heterocycles **2**.

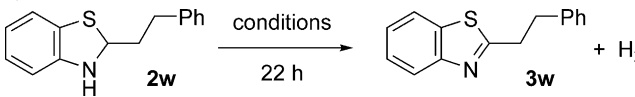
|  |                                                                                               |                                                                                                                    |
|------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|
| Entry                                                                              | N-heterocycle ( <b>2</b> )                                                                    | Product ( <b>3</b> ): Yield [%]                                                                                    |
|                                                                                    |             |                                                                                                                    |
| 1                                                                                  | <b>2a</b> : R <sup>1</sup> = Me, R <sup>2</sup> = H                                           | <b>3a</b> : 92                                                                                                     |
| 2                                                                                  | <b>2b</b> : R <sup>1</sup> = Bu, R <sup>2</sup> = H                                           | <b>3b</b> : 98                                                                                                     |
| 3                                                                                  | <b>2c</b> : R <sup>1</sup> = Ph, R <sup>2</sup> = H                                           | <b>3c</b> : 90                                                                                                     |
| 4                                                                                  | <b>2d</b> : R <sup>1</sup> = 4-MeC <sub>6</sub> H <sub>4</sub> , R <sup>2</sup> = H           | <b>3d</b> : quant.                                                                                                 |
| 5                                                                                  | <b>2e</b> : R <sup>1</sup> = 4-ClC <sub>6</sub> H <sub>4</sub> , R <sup>2</sup> = H           | <b>3e</b> : 85                                                                                                     |
| 6                                                                                  | <b>2f</b> : R <sup>1</sup> = 4-SMeC <sub>6</sub> H <sub>4</sub> , R <sup>2</sup> = H          | <b>3f</b> : 67                                                                                                     |
| 7                                                                                  | <b>2g</b> : R <sup>1</sup> = Me, R <sup>2</sup> = Me                                          | <b>3g</b> : 91                                                                                                     |
| 8                                                                                  | <b>2h</b> : R <sup>1</sup> = Me, R <sup>2</sup> = OMe                                         | <b>3h</b> : 70                                                                                                     |
| 9                                                                                  | <b>2i</b> : R <sup>1</sup> = Me, R <sup>2</sup> = F                                           | <b>3i</b> : 96                                                                                                     |
| 10                                                                                 | <b>2j</b> : R <sup>1</sup> = Me, R <sup>2</sup> = Cl                                          | <b>3j</b> : 90                                                                                                     |
| 11                                                                                 | <b>2k</b> : R <sup>1</sup> = Me, R <sup>2</sup> = Br                                          | <b>3k</b> : 89                                                                                                     |
| 12                                                                                 |  <b>2l</b> |  <b>3l</b> : 70                 |
| 13                                                                                 |  <b>2m</b> |  <b>3m</b> : 90 <sup>[a]</sup> |
|                                                                                    |          |                               |
| 14                                                                                 | <b>2n</b> : R <sup>3</sup> = Me                                                               | <b>3n</b> : 93                                                                                                     |
| 15                                                                                 | <b>2o</b> : R <sup>3</sup> = Ph                                                               | <b>3o</b> : 71                                                                                                     |
|                                                                                    |          |                               |
| 16                                                                                 | <b>2p</b> : R <sup>4</sup> = H, R <sup>5</sup> = H                                            | <b>3p</b> : 45 <sup>[b]</sup>                                                                                      |
| 17                                                                                 | <b>2q</b> : R <sup>4</sup> = Me, R <sup>5</sup> = H                                           | <b>3q</b> : 90                                                                                                     |
| 18                                                                                 | <b>2r</b> : R <sup>4</sup> = H, R <sup>5</sup> = Me                                           | <b>3r</b> : 91                                                                                                     |
|                                                                                    |          |                               |
| 19                                                                                 | <b>2s</b> : R <sup>6</sup> = Me                                                               | <b>3s</b> : 75 <sup>[a]</sup>                                                                                      |
| 20                                                                                 | <b>2t</b> : R <sup>6</sup> = Ph                                                               | <b>3t</b> : 91                                                                                                     |
|                                                                                    |          |                               |
| 21                                                                                 | <b>2u</b> : R <sup>7</sup> = Ph                                                               | <b>3u</b> : 91 <sup>[a]</sup>                                                                                      |
| 22                                                                                 | <b>2v</b> : R <sup>7</sup> = 1-naph                                                           | <b>3v</b> : 92 <sup>[a]</sup>                                                                                      |
| 23                                                                                 | <b>2w</b> : R <sup>7</sup> = CH <sub>2</sub> CH <sub>2</sub> Ph                               | <b>3w</b> : 74 <sup>[a]</sup>                                                                                      |

Yield is that of the isolated product. [a] 10 mol % of **1a** was used. [b] The reaction was run for 48 hours.

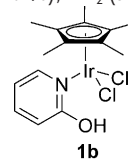
respectively, in high yield, thus requiring only a slight modification to the optimal reaction conditions (entries 19 and 20). Benzothiazoles represent another ubiquitous structural motif in pharmaceuticals and their synthesis by the dehydrogenation of thiazoline has been widely investigated. Because of the presence of sulfur atoms in benzothiazoles, catalyst poisoning presents a severe synthetic obstacle, and the acceptorless dehydrogenation of thiazoline using homogeneous metal catalysts remains to be achieved. However, in the presence of 10 mol % of **1a**, the dehydrogenative synthesis of benzothiazoles was accomplished in good to excellent yield (entries 21–23).

The catalytic dehydrogenation of **2w** is particularly challenging using either [Cp\*Ir(2-hydroxypyridine)]<sup>[5a]</sup> or quinone-catalyzed transition-metal-free aerobic conditions,<sup>[1f]</sup> thus providing **3w** in 38 and 7% yield, respectively (Table 2, entries 2 and 3). In comparison to conventional acceptorless or aerobic dehydrogenation catalysts, these results clearly demonstrate the exceptionally high tolerance of **1a** toward sulfur functionalities.

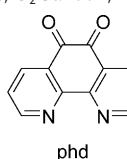
**Table 2:** Comparison of the catalytic dehydrogenation activity for the synthesis of the benzothiazole **3w**.



| Entry | Conditions                                                                   | Yield [%] |
|-------|------------------------------------------------------------------------------|-----------|
| 1     | <b>1a</b> (10 mol %), <i>p</i> -xylene, 150 °C                               | 74        |
| 2     | <b>1b</b> (10 mol %), <i>p</i> -xylene, 150 °C                               | 38        |
| 3     | phd (10 mol %), ZnI <sub>2</sub> (5 mol %), O <sub>2</sub> balloon, MeCN, RT | 7         |



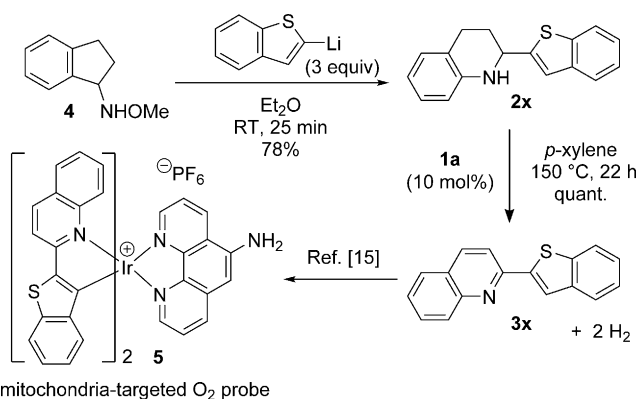
**1b**



phd

Yield is that of the isolated product.

To assess the synthetic utility of this borane-catalyzed dehydrogenation method, we applied our protocol to the synthesis of a functional molecule (Scheme 2). Tobita and co-workers reported that the iridium complex **5** acts as a mitochondria-targeted oxygen probe in HeLa cells.<sup>[15]</sup> Although the  $\pi$ -extended heterobiaryl ligand **3x** can be synthesized by palladium-catalyzed Suzuki coupling, the risk of contamination with toxic palladium should be avoided in the context of biological applications. We envisaged that the transition-metal-free synthesis of this heterobiaryl might be accomplished by the catalytic dehydrogenation of the corresponding partially saturated N-heterocycle. Following the method reported by Miyata and co-workers,<sup>[16]</sup> treatment of the readily available hydroxylamine methyl ether **4** with the respective organolithium reagent afforded the 2-heteroaryl 1,2,3,4-tetrahydroquinoline **2x** in 78% yield. The subsequent catalytic dehydrogenation of **2x** with 10 mol % of **1a** afforded the heterobiaryl **3x** in quantitative yield. This highly efficient transition-metal-free method may thus serve as a new route to



**Scheme 2.** Transition-metal-free synthesis of the heterobiaryl **3x** by catalytic dehydrogenation.

2-substituted quinolines, which are not only interesting from a materials science perspective, but also for the synthesis of biologically active substances.

In summary, we have established a borane-catalyzed metal-free acceptorless dehydrogenation of N-heterocycles. As these borane catalysts are less toxic<sup>[17]</sup> and more accessible than transition-metal complexes, and also exhibit an unprecedented chemoselectivity toward a broader range of N-heterocyclic substrates, the present metal-free dehydrogenation protocol offers explicit advantages relative to transition metal catalyzed reactions. The method reported herein thus represents the first example for a borane-catalyzed acceptorless dehydrogenation in organic synthesis. This reaction thus uncovers a new aspect of borane-mediated catalysis in synthetic organic chemistry. Further expansion of the substrate scope, a detailed mechanistic analysis,<sup>[18]</sup> and the application of this borane-mediated catalysis to the functionalization of sp<sup>3</sup> C–H bonds are currently in progress in our laboratory.

## Acknowledgments

This research was supported in part by the ERATO program of JST (M.Ka.). M.Ko. thanks the Graduate Program for Leaders in Life Innovation (GPLLI) and the JSPS for fellowships.

**Keywords:** boron · heterocycles · homogeneous catalysis · hydrogen · synthetic methods

**How to cite:** *Angew. Chem. Int. Ed.* **2016**, 55, 12224–12227  
*Angew. Chem.* **2016**, 128, 12412–12415

- [1] For related reviews, see: a) C. A. Girard, H. Huang, F. Zhou, G.-J. Deng, C.-J. Li, *Org. Chem. Front.* **2015**, 2, 279; b) G. X. Giustra, J. S. A. Ishibashi, S.-Y. Liu, *Coord. Chem. Rev.* **2016**, 314, 134. For selected examples, see: c) S.-I. Murahashi, Y. Okano, H. Sato, T. Nakae, N. Komiya, *Synlett* **2011**, 1675; d) H. Yuan, W.-J. Yoo, H. Miyamura, S. Kobayashi, *J. Am. Chem. Soc.* **2012**, 134, 13970; e) H. Yuan, W.-J. Yoo, H. Miyamura, S. Kobayashi, *Adv. Synth. Catal.* **2012**, 354, 2899; f) A. E. Wendlandt, S. S. Stahl, *J. Am. Chem. Soc.* **2014**, 136, 506; g) A. E.

- Wendlandt, S. S. Stahl, *J. Am. Chem. Soc.* **2014**, *136*, 11910; h) A. V. Iosub, S. S. Stahl, *Org. Lett.* **2015**, *17*, 4404; i) X. Cui, Y. Li, S. Bachmann, M. Scalone, A.-E. Surkus, K. Junge, C. Topf, M. Beller, *J. Am. Chem. Soc.* **2015**, *137*, 10652.
- [2] B. M. Trost, *Science* **1991**, *254*, 1471.
- [3] a) C. Gunanathan, D. Milstein, *Science* **2013**, *341*, 249. Catalytic acceptorless dehydrogenation of N-heterocycles is also a key reaction in hydrogen storage technology. For related reviews, see: b) R. H. Crabtree, *Energy Environ. Sci.* **2008**, *1*, 134; c) Q.-L. Zhu, Q. Xu, *Energy Environ. Sci.* **2015**, *8*, 478.
- [4] For selected reviews of ruthenium-catalyzed acceptorless dehydrogenation of organic compounds, see: a) C. Gunanathan, D. Milstein, *Chem. Rev.* **2014**, *114*, 12024; b) S. Werkmeister, J. Neumann, K. Junge, M. Beller, *Chem. Eur. J.* **2015**, *21*, 12226. For selected examples, see: c) S. Muthaiah, S. H. Hong, *Adv. Synth. Catal.* **2012**, *354*, 3045; d) M. Zhang, X. Fang, H. Neumann, M. Beller, *J. Am. Chem. Soc.* **2013**, *135*, 11384; e) M. Nielsen, E. Alberico, W. Baumann, H.-J. Drexler, H. Junge, S. Gladiali, M. Beller, *Nature* **2013**, *495*, 85; f) M. Chen, M. Zhang, B. Xiong, Z. Tan, W. Lv, H. Jiang, *Org. Lett.* **2014**, *16*, 6028; g) A. Khalafi-Nezhad, F. Panahi, *ACS Catal.* **2014**, *4*, 1686.
- [5] a) R. Yamaguchi, C. Ikeda, Y. Takahashi, K. Fujita, *J. Am. Chem. Soc.* **2009**, *131*, 8410; b) J. Wu, D. Talwar, S. Johnston, M. Yan, J. Xiao, *Angew. Chem. Int. Ed.* **2013**, *52*, 6983; *Angew. Chem.* **2013**, *125*, 7121; c) K. Fujita, Y. Tanaka, M. Kobayashi, R. Yamaguchi, *J. Am. Chem. Soc.* **2014**, *136*, 4829; d) S. Chakraborty, W. W. Brennessel, W. D. Jones, *J. Am. Chem. Soc.* **2014**, *136*, 8564; e) M. G. Manas, L. S. Sharninghausen, E. Lin, R. H. Crabtree, *J. Organomet. Chem.* **2015**, *792*, 184; f) R. Xu, S. Chakraborty, H. Yuan, W. D. Jones, *ACS Catal.* **2015**, *5*, 6350; g) D. Talwar, A. Gonzalez-de-Castro, H. Y. Li, J. Xiao, *Angew. Chem. Int. Ed.* **2015**, *54*, 5223; *Angew. Chem.* **2015**, *127*, 5312. A related catalytic acceptorless dehydrogenation of heterocycles was also reported by Nozaki, see: h) S. Kusumoto, M. Akiyama, K. Nozaki, *J. Am. Chem. Soc.* **2013**, *135*, 18726.
- [6] For selected reviews, see: a) D. W. Stephan, *Org. Biomol. Chem.* **2008**, *6*, 1535; b) D. W. Stephan, G. Erker, *Angew. Chem. Int. Ed.* **2010**, *49*, 46; *Angew. Chem.* **2010**, *122*, 50; c) D. W. Stephan, *J. Am. Chem. Soc.* **2015**, *137*, 10018; d) D. W. Stephan, *Acc. Chem. Res.* **2015**, *48*, 306; e) D. W. Stephan, G. Erker, *Angew. Chem. Int. Ed.* **2015**, *54*, 6400; *Angew. Chem.* **2015**, *127*, 6498.
- [7] For selected reviews on FLP-mediated hydrogenations, see: a) D. W. Stephan, S. Greenberg, T. W. Graham, P. Chase, J. J. Hastie, S. J. Geier, J. M. Farrell, C. C. Brown, Z. M. Heiden, G. C. Welch, M. Ullrich, *Inorg. Chem.* **2011**, *50*, 12338; b) D. W. Stephan, *Org. Biomol. Chem.* **2012**, *10*, 5740; c) J. Paradies, *Synlett* **2013**, 777; d) J. Paradies, *Angew. Chem. Int. Ed.* **2014**, *53*, 3552; *Angew. Chem.* **2014**, *126*, 3624; e) X. Feng, H. Du, *Tetrahedron Lett.* **2014**, *55*, 6959; f) L. J. Hounjet, D. W. Stephan, *Org. Process Res. Dev.* **2014**, *18*, 385; g) M. Oestreich, J. Hermeke, J. Mohr, *Chem. Soc. Rev.* **2015**, *44*, 2202; h) J. Mohr, D. Porwal, I. Chatterjee, M. Oestreich, *Chem. Eur. J.* **2015**, *21*, 17583. For selected examples on the hydrogenation of C=N bonds, see: i) P. A. Chase, G. C. Welch, T. Jurca, D. W. Stephan, *Angew. Chem. Int. Ed.* **2007**, *46*, 8050; *Angew. Chem.* **2007**, *119*, 8196; j) P. A. Chase, T. Jurca, D. W. Stephan, *Chem. Commun.* **2008**, 1701; k) P. Spies, S. Schwendemann, S. Lange, G. Kehr, R. Fröhlich, G. Erker, *Angew. Chem. Int. Ed.* **2008**, *47*, 7543; *Angew. Chem.* **2008**, *120*, 7654; l) V. Sumerin, F. Schultz, M. Atsumi, C. Wang, M. Nieger, M. Leskelä, T. Repo, P. Pykkö, B. Rieger, *J. Am. Chem. Soc.* **2008**, *130*, 14117; m) D. Chen, J. Klankermayer, *Chem. Commun.* **2008**, 2130; n) G. Erős, H. Mehdi, I. Pápai, T. A. Rokob, P. Király, G. Tárkányi, T. Soós, *Angew. Chem. Int. Ed.* **2010**, *49*, 6559; *Angew. Chem.* **2010**, *122*, 6709; o) S. J. Geier, P. A. Chase, D. W. Stephan, *Chem. Commun.* **2010**, 46, 4884; p) D. Chen, Y. Wang, J. Klankermayer, *Angew. Chem. Int. Ed.* **2010**, *49*, 9475; *Angew. Chem.* **2010**, *122*, 9665; q) T. Mahdi, Z. M. Heiden, S. Grimme, D. W. Stephan, *J. Am. Chem. Soc.* **2012**, *134*, 4088; r) Y. Liu, H. Du, *J. Am. Chem. Soc.* **2013**, *135*, 6810; s) Y. Liu, H. Du, *J. Am. Chem. Soc.* **2013**, *135*, 12968; t) D. J. Scott, M. J. Fuchter, A. E. Ashley, *Angew. Chem. Int. Ed.* **2014**, *53*, 10218; *Angew. Chem.* **2014**, *126*, 10382; u) J. Mohr, M. Oestreich, *Angew. Chem. Int. Ed.* **2014**, *53*, 13278; *Angew. Chem.* **2014**, *126*, 13494; v) Z. Zhang, H. Du, *Angew. Chem. Int. Ed.* **2015**, *54*, 623; *Angew. Chem.* **2015**, *127*, 633; w) J. M. Farrell, R. T. Posaratnanathan, D. W. Stephan, *Chem. Sci.* **2015**, *6*, 2010; x) P. Eisenberger, B. P. Bestvater, E. C. Keske, C. M. Crudden, *Angew. Chem. Int. Ed.* **2015**, *54*, 2467; *Angew. Chem.* **2015**, *127*, 2497; y) M. Lindqvist, K. Borre, K. Axenov, B. Kótai, M. Nieger, M. Leskelä, I. Pápai, T. Repo, *J. Am. Chem. Soc.* **2015**, *137*, 4038.
- [8] For related precedents, see: a) A. J. M. Miller, J. E. Bercaw, *Chem. Commun.* **2010**, 46, 1709; b) C. Appelt, J. C. Sloatweg, K. Lammertsma, W. Uhl, *Angew. Chem. Int. Ed.* **2013**, *52*, 4256; *Angew. Chem.* **2013**, *125*, 4350; c) Z. Lu, L. Schweighauser, H. Hausmann, H. A. Wegner, *Angew. Chem. Int. Ed.* **2015**, *54*, 15556; *Angew. Chem.* **2015**, *127*, 15777; d) Z. Mo, A. Rit, J. Campos, E. L. Kolychev, S. Aldridge, *J. Am. Chem. Soc.* **2016**, *138*, 3306.
- [9] For selected examples of hydride abstraction from organic molecules by the electrophilic borane, see: a) N. Millot, C. C. Santini, B. Fenet, J. M. Basset, *Eur. J. Inorg. Chem.* **2002**, 3328; b) J. M. Farrell, Z. M. Heiden, D. W. Stephan, *Organometallics* **2011**, *30*, 4497; c) J. D. Webb, V. S. Laberge, S. J. Geier, D. W. Stephan, C. M. Crudden, *Chem. Eur. J.* **2010**, *16*, 4895; d) I. Chatterjee, M. Oestreich, *Angew. Chem. Int. Ed.* **2015**, *54*, 1965; *Angew. Chem.* **2015**, *127*, 1988; e) I. Chatterjee, Z.-W. Qu, S. Grimme, M. Oestreich, *Angew. Chem. Int. Ed.* **2015**, *54*, 12158; *Angew. Chem.* **2015**, *127*, 12326; f) A. Simonneau, M. Oestreich, *Angew. Chem. Int. Ed.* **2013**, *52*, 11905; *Angew. Chem.* **2013**, *125*, 12121; g) S. Keess, A. Simonneau, M. Oestreich, *Organometallics* **2015**, *34*, 790. For a related review, see: h) F. Focante, P. Mercandelli, A. Sironi, L. Resconi, *Coord. Chem. Rev.* **2006**, *250*, 170. Borane-catalyzed hydride abstraction is also a key step in transfer hydrosilylation chemistry. For a review, see: i) M. Oestreich, *Angew. Chem. Int. Ed.* **2016**, *55*, 494; *Angew. Chem.* **2016**, *128*, 504.
- [10] For details, see section 4 of the Supporting Information.
- [11] For details, see section 3 of the Supporting Information.
- [12] M. Ahmed Ibrahim, *Heterocycles* **2011**, *83*, 2689.
- [13] D. Liu, G. Zhao, L. Xiang, *Eur. J. Org. Chem.* **2010**, 3975.
- [14] T. D. Penning, J. J. Talley, S. R. Bertenshaw, J. S. Carter, P. W. Collins, S. Docter, M. J. Graneto, L. F. Lee, J. W. Malecha, J. M. Miyashiro, R. S. Rogers, D. J. Rogier, S. S. Yu, G. D. Anderson, E. G. Burton, J. N. Cogburn, S. A. Gregory, C. M. Koboldt, W. E. Perkins, K. Seibert, A. W. Veenhuizen, Y. Y. Zhang, P. C. Isakson, *J. Med. Chem.* **1997**, *40*, 1347.
- [15] T. Yoshihara, S. Murayama, T. Masuda, T. Kikuchi, K. Yoshida, M. Hosaka, S. Tobita, *J. Photochem. Photobiol. A* **2015**, *299*, 172.
- [16] M. Ueda, S. Kawai, M. Hayashi, T. Naito, O. Miyata, *J. Org. Chem.* **2010**, *75*, 914.
- [17] According to the ICH harmonized guideline for elemental impurities, the permitted concentrations for palladium or iridium in drug products for parenteral dose is 1 µg g<sup>-1</sup>. A value for boron has not been established because of its inherently low toxicity. For details, see: <https://www.pmda.go.jp/files/000197758.pdf> (accessed on 13 June 2016).
- [18] For mechanistic discussions, see section 3 of the Supporting Information.

Received: June 25, 2016

Revised: July 24, 2016

Published online: August 19, 2016