JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
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Chiral Molecular Tweezers: Synthesis and Reactivity in Asymmetric Hydrogenation

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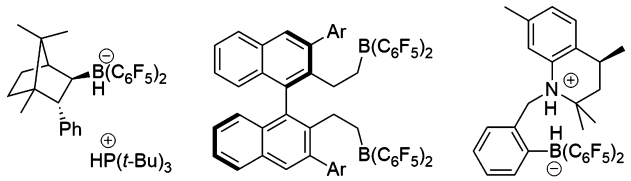
Supporting Information

ABSTRACT: We report the synthesis and reactivity of a chiral aminoborane displaying both rapid and reversible H_2 activation. The catalyst shows exceptional reactivity in asymmetric hydrogenation of enamines and unhindered imines with stereoselectivities of up to 99% ee. DFT analysis of the reaction mechanism pointed to the importance of both repulsive steric and stabilizing intermolecular non-covalent forces in the stereodetermining hydride transfer step of the catalytic cycle.

One of the most efficient and atom-economical ways to prepare chiral amines is by transition metal (TM)-catalyzed asymmetric hydrogenation of prochiral imines and enamines.[1] The products, having chiral α-carbons, are important in synthetic chemistry because of their applications as ligands, resolving agents, chiral auxiliaries, and building blocks. Also, the chiral information and tendency to form H-bonds are essential features in molecular recognition, making them potential pharmaceuticals.[2] Preparation of drugs via TM catalysis requires tedious product purification because of strict demands on heavy-metal residuals in the products.[3]

Recently, main-group systems combining sterically hindered Lewis acids and bases have been reported to cleave molecular hydrogen heterolytically under mild reaction conditions.[4] The chemistry of these "frustrated Lewis pairs" (FLPs) has attracted increased scientific and practical interest, mainly because of their applicability as catalysts in homogeneous metal-free hydrogenations of imines, enamines,[5] N-heterocycles,[6] and carbonyl compounds.[7] In this regard, it is surprising that reports of the corresponding asymmetric reactions are still few. Intermolecular FLP systems involving chiral boranes have been successfully utilized for enantioselective imine hydrogenation. The use of inherently chiral terpene groups (e.g., α-pinene and camphor) on boron (**1** in Figure 1) has proven to be effective for hydrogenation of acetophenone *N*-arylimines, and ee's of up to 83% were reported.[8] A recent development was achieved by introducing chirality through a binaphthyl backbone (**2**), enabling hydrogenation of imines, silyl enol ethers, and 2,3-disubstituted quinoxalines at room temperature with high asymmetric induction.[9]

In intramolecular FLP systems, appropriate linking of the Lewis acid and base has proven to be crucial for H_2 activation as well as for the hydrogen transfer process.[10] In *ansa*-aminoboranes, the Lewis acid and base are in close vicinity, but bulky substituents hinder dative bond formation. Such structures generate high FLP reactivity, allowing the substrate scope to be expanded to enamines and *N*-alkyl imines.[5d,11] However, previous attempts to incorporate the high reactivity of *ansa*-aminoboranes and asymmetric hydrogenation, namely, the introduction of chiral amines into linked systems via straightforward synthetic approaches (**3** in Figure 1), have resulted in only moderate enantioselectivities.[11] Herein we report the synthesis of a chiral binaphthyl-linked aminoborane, its unique reactivity in enantioselective asymmetric hydrogenation of unhindered imines and enamines, and a computational study of the mechanism of these reactions.



1 (up to 83% ee)[8b] **2** (up to 89% ee)[9] **3** (up to 35% ee)[11]

Figure 1. FLP catalysts for asymmetric hydrogenation of imines.

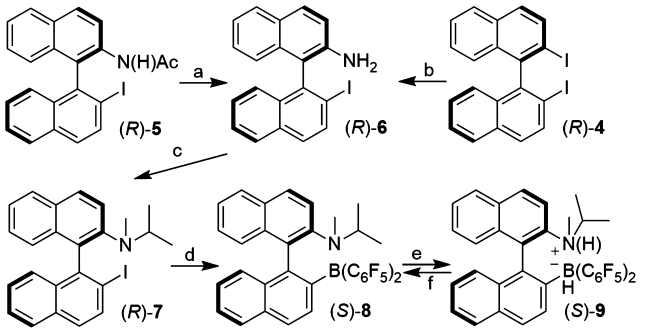
In our catalyst design, the main objective was to introduce the Lewis acid and base groups at the 2- and 2′-positions of the rigid asymmetric binaphthyl core, fixing their positions next to the asymmetric axis and ensuring the close proximity of the amine and boron centers [(*S*)-**8** in Scheme 1]. Another clear benefit of the design is the stability of the arene C−B bond, which impedes retro-hydroboration and decomposition to olefins and aminoboranes, unlike the alkyl-linked analogues.[12] This is an evident advantage, yet few reported examples of chiral biaryls with $-B(C_6F_5)_2$ groups at the 2-position exist.[13]

Following the reported synthetic procedure for (*R*)-2′-iodo-*N*-isopropyl-*N*-methyl-[1,1′-binaphth-2-yl]amine [(*R*)-**7**][14] yielded the product with 82% ee (Scheme 1b,c), as compound **4** has a tendency to racemize during Pd-catalyzed reactions.[15] Therefore, a synthetic route via (*R*)-**5**, which could be isolated in good yield and enantiopurity, was designed.[16] Removal of the acetyl group of (*R*)-**5** with concentrated hydrochloric acid followed by consecutive primary amine alkylations with *i*-PrI and

Received: December 22, 2014
Published: January 30, 2015

DOI: 10.1021/ja512658m
J. Am. Chem. Soc. 2015, 137, 4038−4041

Scheme 1. Synthetic Routes to Enantiopure Catalyst (*S*)-9



(a) EtOH, conc. HCl, 2 h, reflux. (b) $Ph_2C{=}NH$, NaO*t*-Bu, cat. $Pd_2(dba)_3$ + dppe, PhMe, 16 h, 100 °C. (c) (1) *i*-PrI (2 equiv), K_2CO_3 (2 equiv), ACN, 48 h, 120 °C; (2) MeI (2 equiv), K_2CO_3 (2 equiv), ACN, 16 h, 60 °C. (d) (1) −78 °C to RT, PhMe, *n*-BuLi (1 equiv), 3 h; (2) −78 °C to RT, $B(C_6F_5)_2Cl$ (1 equiv), PhMe, 16 h. (e) H_2 (2 bar), PhMe, 1 min, RT. (f) C_6D_6, 15 min, 80 °C.

CH_3I afforded the desired product (*R*)-**7** with high enantiopurity (99% ee according to HPLC). Finally, aminoborane (*S*)-**8** was synthesized by straightforward lithiation and reaction with $B(C_6F_5)_2Cl$ and isolated as its ammonium borohydride salt (*S*)-**9** after heterolytic splitting of H_2.[17]

NMR spectroscopic data for (*S*)-**9** revealed a single species with a ^{11}B NMR signal at −19.3 ppm (doublet, $^1J_{BH}$ = 80.8 Hz), typical for four-coordinate borates. Two different sets of peaks were detected in the ^{19}F NMR spectrum arising from the diastereotopic pentafluorophenyl groups, both having typical borate pattern and thus confirming the assigned structure ($\Delta\delta_{p,m}$ = 2.98 ppm; $\Delta\delta_{p',m'}$ = 3.43 ppm). In the ^1H NMR spectrum, B−*H* was observed as a broad quartet in the region 3.50−2.75 ppm and the ammonium group as a broad singlet at 8.68 ppm, also giving rise to doublet splitting on the N−*Me* group (δ_H = 1.18 ppm, $^1J_{HH}$ = 6.8 Hz). As a result of diastereotopism, the isopropyl group was detected as two methyl doublets separated by 0.49 ppm. Formation of a chiral center on the ammonium nitrogen is possible, yet no evident diastereomers or epimerization was detected spectroscopically.

The X-ray crystallographic study of (*S*)-**9** showed a twisted binaphthyl core with a dihedral angle of 74.3° (Figure 2). This sets the Lewis acid and base close to each other in space, even though they are separated by five bonds. The boron center is sterically well-protected by the diastereotopic pentafluorophenyl groups, which are oriented edge-to-face and adapt pseudoaxial and pseudoequatorial configurations, an arrangement thought to induce high enantioselectivity in chiral biphenyl diphosphine ligand systems.[18] The −N(*i*-Pr) moiety forms a 80.9° angle with the naphthyl plane, resulting in an N−H···H−B torsional angle of 142° yet maintaining a short H···H distance of 1.86 Å.[19]

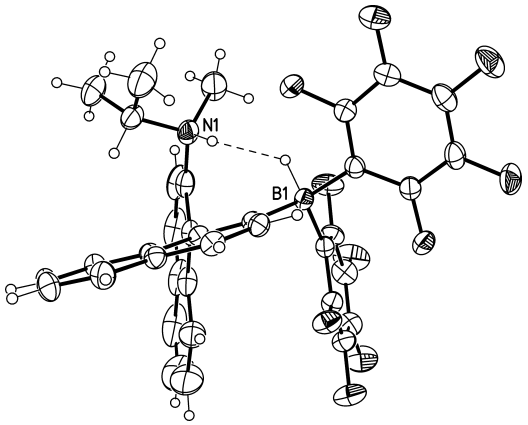
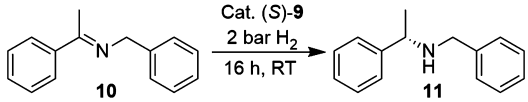


Figure 2. Crystal structure of (*S*)-**9** (50% probability ellipsoids, solvent molecule omitted for clarity).

The formation of colorless (*S*)-**9** upon exposure of deep-red (*S*)-**8** to H_2 was rapid, with quantitative conversion occurring in less than 1 min, making it one of the fastest reactions we have studied in FLP H_2 activation (Scheme 1e). Quantitative dehydrogenation of (*S*)-**9** occurred within 15 min at 80 °C (Scheme 1f).[20] The catalytic activity of (*S*)-**9** was studied, and the reaction conditions were optimized in a series of hydrogenation experiments with substrate **10** (Table 1). With a catalyst loading of 10 mol % in toluene, the reaction at room temperature under H_2 at 2 bar gave 28% conversion in 16 h (entry 1). Prolonging the reaction time by a factor of 4 and simultaneously halving the catalyst loading nearly doubled the conversion, confirming the catalyst's stability (entry 2). Quantitative hydrogenations were observed at elevated temperatures, but with only moderate ee (entry 3). Aiming for higher reaction rate and enantioselectivity, we varied the solvent. As shown earlier,[11] a remarkable increase in activity and enantioselectivity was detected in ethereal solvents (cf. entries 1 and 4). The reaction rate in methyl *tert*-butyl ether (MTBE) was superior relative to diethyl ether, while the enantioselectivity remained unchanged (cf. entries 5 and 6). Finally, a conversion of 94% with 83% ee could be obtained with substrate **10** using 7.5 mol % catalyst (entry 7).

Table 1. Catalytic Hydrogenation of Imine 10 by (*S*)-9 under Different Reaction Conditions



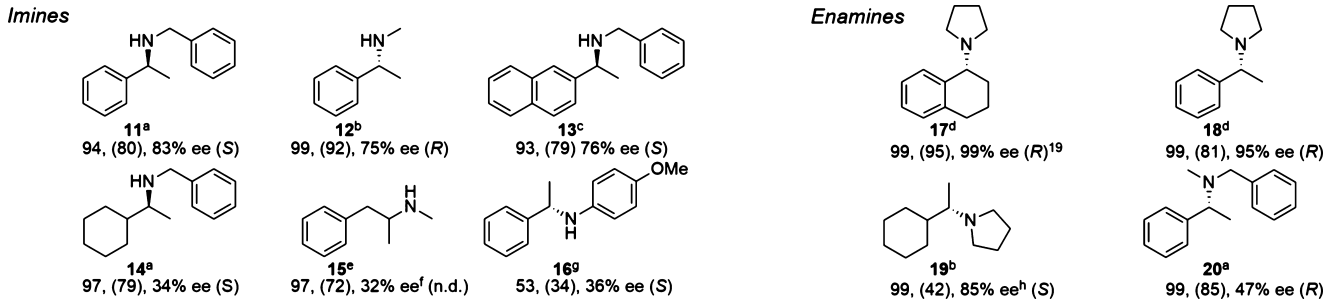
entry	cat. mol %	solvent	conv. [%][a]	ee [%][b]
1	10	PhMe	28	n.d.
2[c]	5	PhMe	48	n.d.
3[d]	10	PhMe	99	41
4	10	Et_2O	99	74
5	5	Et_2O	34	75
6	5	MTBE	56	77
7[e]	7.5	MTBE	94	83

Conditions: (*S*)-**9** (0.01−0.02 mmol), **10** (42 mg, 0.2 mmol), solvent (1 mL). [a]By ^1H NMR spectroscopy. [b]By HPLC (Chiralcel OD-H column). [c]Reaction time 64 h. [d]Reaction temperature 80 °C. [e]Reaction time 20 h.

To continue our experimental investigation, we studied the reactivity of (*S*)-**9** with a range of different substrates (Table 2). Various *N*-alkyl and *N*-benzyl alkyl aryl ketimines were hydrogenated with 75−83% ee, independent of the size of the N substituent (**11**−**13**). The FLP activity was remarkably high with small *N*-methyl imines, despite the production of small amines that commonly reduce the activity by forming deactivating B−N adducts (**12** and **15**). Bulkier *N*-benzyl imine substrates, requiring increased catalyst loading and longer reaction times, also gave products in high yield and enantiopurity (**11**, **13**, and **14**). The most sterically encumbered and least basic imine in our series [*N*-(*p*-methoxyphenyl) acetophenone imine] was not reduced quantitatively even at elevated temperatures,

DOI: 10.1021/ja512658m
J. Am. Chem. Soc. 2015, 137, 4038−4041

Table 2. Catalytic Asymmetric Hydrogenations of Imines and Enamines Catalyzed by (*S*)-9



^{1}H NMR conversion [%], (isolated yield [%]), ee by HPLC (Chiralcel OD-H or OD-J column). Conditions: H_2 (2 bar), substrate (200 μmol), MTBE (1 mL), 25 °C. [a](*S*)-**9** (15 μmol), 20 h. [b](*S*)-**9** (5 μmol), 16 h. [c](*S*)-**9** (10 μmol), 20 h. [d](*S*)-**9** (5 μmol), 0.5 h. [e](*S*)-**9** (10 μmol), 16 h. [f]ee by ^{1}H NMR as diastereomers with *O*-acetylmandelic acid. [g](*S*)-**9** (20 μmol), 60 °C, 64 h, PhMe solvent. [h]ee by optical rotation.

and product **16** was obtained in 53% conversion. These results describe an interesting reverse substrate preference of (*S*)-**9** in comparison to previous FLP catalysts and are a fingerprint of an exceptionally hindered borane (see Figure 2).[11]

Although (*S*)-**9** prefers small imines for hydrogenation, stereoselective hydrogenation of alkyl imines remains challenging because of the chemically similar groups on both sides of the C═N carbon. Catalyst (*S*)-**9** yielded alkyl amines **14** and **15** with over 30% ee, which are noteworthy values compared with previous FLP results.[9a,11]

Remarkably, *N*,*N*-symmetric enamines were quantitatively converted to the corresponding amines with extremely high optical purity (**17** and **18**). Alkyl amine **19** was also obtained with high optical purity (85% ee). Unequal *N*-alkyl groups decreased the enantioselectivity due to iminium intermediate formation and the possibility of *E*/*Z* isomerism (**20**). The results with *N*,*N*-dialkyl enamines are particularly important, as they are among the most challenging substrates for TM catalysts.[1b]

To gain insight into the mechanism of the present hydrogenation reactions and the origin of the observed stereoselectivity, we explored possible reaction pathways for the formation of amine **17** in a computational study. We used density functional theory (DFT) calculations to identify and characterize relevant transition states and the corresponding reaction intermediates.[21] The results are summarized in terms of a free energy diagram as depicted in Figure 3. In line with our experimental observations, the calculations predicted a fairly low barrier (14.7 kcal/mol) for the heterolytic H_2 splitting induced by aminoborane (*S*)-**8** (denoted as **cat** in Figure 3). This reaction

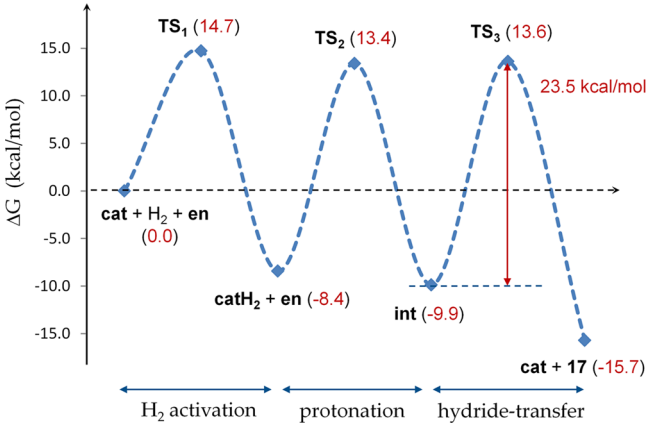


Figure 3. Computed free energy diagram for the formation of **17**.

was found to be clearly exergonic under standard conditions, but the reverse process (H_2 elimination) becomes feasible at higher temperatures using nonpolar solvents.[22]

The computational results support the view that hydrogen transfer from the hydrogenated FLP to the enamine occurs in two distinct steps: it is initiated by protonation of the substrate, which is followed by a hydride transfer process.[23] The barrier for the latter step was found to be slightly higher than that of the protonation (23.5 and 21.8 kcal/mol, respectively) suggesting that the hydride transfer is likely to be rate-determining in the catalytic cycle. The most stable form of the hydridoborate/iminium ion-pair intermediate formed upon protonation was computed to have a free energy of −9.9 kcal/mol (see **int** in Figure 3), but several other low-lying and easily interchangeable forms could be identified for this species. These isomeric forms differ in the orientation of the aryl substituents at the boron center and also in the relative position of the interacting iminium ion. The BH^- unit of the hydridoborate species is embedded in a chiral environment, which enables stereoselective attack of the iminium ion. Hydride transfer to the *Re* face of the iminium was predicted to be kinetically favored (by 1.4 kcal/mol) over the attack at the *Si* face, which is consistent with the observed enantioselectivity (excess of the *R* product). Our analysis of the origin of the stereoselectivity revealed that the energy difference obtained for the competing transition states is a result of a subtle balance between repulsive steric and attractive non-covalent interactions in the stereoselectivity-determining hydride transfer step (see Figure 4 and the Supporting Information).

In summary, a chiral bridged binaphthyl aminoborane catalyst for highly enantioselective hydrogenation is reported. A series of imines and enamines react readily under mild conditions with

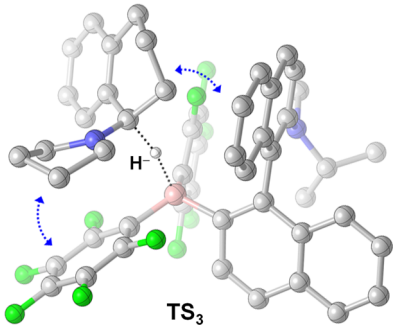


Figure 4. Transition state of the hydride transfer yielding the major product enantiomer. Intermolecular contacts are highlighted by blue arrows. CH hydrogen atoms have been omitted for clarity.

DOI: 10.1021/ja512658m
J. Am. Chem. Soc. 2015, 137, 4038−4041

enantioselectivities of up to 99% ee. Unhindered *N*-alkyl imines are readily hydrogenated without catalyst−product adduct formation, in contrast to what is typical for FLPs. Most importantly, the first results on FLP-catalyzed asymmetric hydrogenations of enamines are presented. Because the catalyst itself can be synthesized from readily available starting materials with high enantiopurity, the simplicity of the synthesis and overall structure makes (*S*)-**9** a good candidate for further development in asymmetric metal-free hydrogenation.

■ ASSOCIATED CONTENT

Supporting Information

Procedures and additional data. This material is available free of charge via the Internet at http://pubs.acs.org. Structure parameters for (*S*)-**9** (CCDC-1036946), (*R*)-**9** (CCDC-1036947), and (*R*)-**17**·HCl (CCDC-1036948) are available from the Cambridge Crystallographic Data Centre.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the Academy of Finland (139550, 276586), the Inorganic Materials Chemistry Graduate Program, COST Action CM0905, and the Hungarian Scientific Research Fund (OTKA, K-81927).

■ REFERENCES

(1) Selected reviews of TM-catalyzed asymmetric hydrogenation of enamines and imines: (a) Spindler, F.; Blaser, H.-U. Enantioselective Hydrogenation of C═N Functions and Enamines. In *Handbook of Homogenous Hydrogenation*; de Vries, J. G., Elsevier, C. J., Eds.; Wiley-VCH: Weinheim, Germany, 2007; Vol. 3, pp 1193−1214. (b) Xie, J.-H.; Zhu, S.-F.; Zhou, Q.-L. *Chem. Rev.* **2011**, *111*, 1713. (c) Yu, Z.; Jin, W.; Jiang, Q. *Angew. Chem., Int. Ed.* **2012**, *51*, 6060. (d) Xie, J.-H.; Zhu, S.-F.; Zhou, Q.-L. *Chem. Soc. Rev.* **2012**, *41*, 4126.

(2) (a) Nugent, T. C. *Chiral Amine Synthesis: Methods, Developments and Applications*; Wiley-VCH: Weinheim, Germany, 2010. (b) Nugent, T. C.; El-Shazly, M. *Adv. Synth Catal.* **2010**, *352*, 753.

(3) (a) Garrett, C. E.; Prasad, K. *Adv. Synth. Catal.* **2004**, *346*, 889. (b) Dalko, P. I.; Moisan, L. *Angew. Chem., Int. Ed.* **2001**, *40*, 3726.

(4) (a) Welch, G. C.; San Juan, R. R.; Masuda, J. D.; Stephan, D. W. *Science* **2006**, *314*, 1124. (b) Stephan, D. W. *Org. Biomol. Chem.* **2008**, *6*, 1535. (c) Stephan, D. W.; Erker, G. *Angew. Chem., Int. Ed.* **2010**, *49*, 171. (d) Powers, P. P. *Nature* **2010**, *463*, 171. (e) Erker, G. *C. R. Chim.* **2011**, *14*, 831. (f) Stephan, D. W. *Org. Biomol. Chem.* **2012**, *10*, 5740. (g) Hounjet, L. J.; Stephan, D. W. *Org. Process Res. Dev.* **2014**, *18*, 385. (h) Paradies, J. *Angew. Chem., Int. Ed.* **2014**, *53*, 3552. (i) Feng, X.; Du, H. *Tetrahedron Lett.* **2014**, *55*, 6959. (j) Shi, L.; Zhou, Y.-G. *ChemCatChem* **2015**, *7*, 54.

(5) (a) Chase, P. A.; Welch, G. C.; Jurca, T.; Stephan, D. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 8050. (b) Spies, P.; Schwendemann, S.; Lange, S.; Kehr, G.; Fröhlich, R.; Erker, G. *Angew. Chem., Int. Ed.* **2008**, *47*, 7543. (c) Chase, P. A.; Jurca, T.; Stephan, D. W. *Chem. Commun.* **2008**, 1701. (d) Sumerin, V.; Schulz, F.; Atsumi, M.; Wang, C.; Nieger, M.; Leskelä, M.; Repo, T.; Pyykkö, P.; Rieger, B. *J. Am. Chem. Soc.* **2008**, *130*, 14117. (e) Jiang, C.; Blacque, O.; Berke, H. *Chem. Commun.* **2009**, 5518. (f) Rokob, T. A.; Hamza, A.; Stirling, A.; Pápai, I. *J. Am. Chem. Soc.* **2009**, *131*, 2029. (g) Axenov, K. V.; Kehr, G.; Frölich, R.; Erker, G. *J. Am. Chem. Soc.* **2009**, *131*, 3454. (h) Axenov, K. V.; Kehr, G.; Frölich, R.; Erker, G. *Organometallics* **2009**, *28*, 5148. (i) Erős, G.; Mehdi, H.; Pápai, I.; Rokob, T. A.; Király, P.; Tárkányi, G.; Soós, T. *Angew. Chem., Int. Ed.* **2010**, *49*, 6559. (j) Farrell, J. M.; Hatnean, J. A.; Stephan, D. W. *J. Am. Chem. Soc.* **2012**, *134*, 15728. (k) Chernichenko, K.; Nieger, M.; Leskelä, M.; Repo, T. *Dalton Trans.* **2012**, *41*, 9029. (l) Wang, G.; Chen, C.; Du, T.; Zhong, W. *Adv. Synth. Catal.* **2014**, *356*, 1747. (m) Hatnean, J. A.; Thomson, J. W.; Chase, P. A.; Stephan, D. W. *Chem. Commun.* **2014**, *50*, 301.

(6) (a) Geier, S. J.; Chase, P. A.; Stephan, D. W. *Chem. Commun.* **2010**, *46*, 4884. (b) Stephan, D. W.; Greenberg, S.; Graham, T. W.; Chase, P.; Hastie, J. J.; Geier, S. J.; Farrell, J. M.; Brown, C. C.; Heiden, Z. M.; Welch, G. C.; Ullrich, M. *Inorg. Chem.* **2011**, *50*, 12338. (c) Erős, G.; Nagy, K.; Pápai, I.; Nagy, P.; Király, G.; Tárkányi, G.; Soós, T. *Chem.—Eur. J.* **2012**, *18*, 574. (d) Scott, D. J.; Fuchter, M. J.; Ashley, A. E. *Angew. Chem., Int. Ed.* **2014**, *53*, 10218. (e) Clark, E. R.; Ingleson, M. J. *Angew. Chem., Int. Ed.* **2014**, *53*, 11306.

(7) (a) Mahdi, T.; Stephan, D. W. *J. Am. Chem. Soc.* **2014**, *136*, 15809. (b) Scott, D. J.; Fuchter, M. J.; Ashley, A. E. *J. Am. Chem. Soc.* **2014**, *136*, 15813.

(8) (a) Chen, D.; Klankermayer, J. *Chem. Commun.* **2008**, 2130. (b) Chen, D.; Wang, Y.; Klankermayer, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 9475. (c) Ghattas, G.; Chen, D.; Pan, F.; Klankermayer, J. *Dalton Trans.* **2012**, *41*, 9026.

(9) (a) Liu, Y.; Du, H. *J. Am. Chem. Soc.* **2013**, *135*, 6810. (b) Wei, S.; Du, H. *J. Am. Chem. Soc.* **2014**, *136*, 12261. (c) Zhang, Z.; Du, H. *Angew. Chem., Int. Ed.* **2015**, *54*, 623.

(10) (a) Rokob, T. A.; Hamza, A.; Pápai, I. *J. Am. Chem. Soc.* **2009**, *131*, 10701. (b) Rokob, T. A.; Pápai, I. *Top. Curr. Chem.* **2013**, *332*, 157.

(11) Sumerin, V.; Chernichenko, K.; Nieger, M.; Leskelä, M.; Rieger, B.; Repo, T. *Adv. Synth. Catal.* **2011**, *353*, 2093.

(12) (a) Singaram, B.; Goralski, C. T.; Rangaishenvi, M. V.; Brown, H. C. *J. Am. Chem. Soc.* **1989**, *111*, 384. (b) Sigaram, B.; Rangaishenvi, M. V.; Brown, H. C.; Goralski, C. T.; Hasha, D. L. *J. Org. Chem.* **1991**, *56*, 1543. (c) Singaram, B.; Goralski, C. T.; Fisher, G. B. *J. Org. Chem.* **1991**, *56*, 5691. (d) Parks, D. J.; Piers, W. E.; Yap, G. P. A. *Organometallics* **1998**, *17*, 5492. (e) Schwendemann, S.; Oishi, S.; Saito, S.; Fröhlich, R.; Kehr, G.; Erker, G. *Chem.—Asian J.* **2013**, *8*, 212. (f) Lindqvist, M.; Axenov, K.; Nieger, M.; Räisänen, M.; Leskelä, M.; Repo, T. *Chem.—Eur. J.* **2013**, *19*, 10412.

(13) Morrison, D. J.; Piers, W. E.; Parvez, M. *Synlett* **2004**, 2429.

(14) García-Fortanet, J.; Kessler, F.; Buchwald, S. L. *J. Am. Chem. Soc.* **2009**, *131*, 6676.

(15) (a) Juríček, M.; Brath, H.; Kasák, P.; Putala, M. *J. Organomet. Chem.* **2007**, *692*, 5279. (b) Brath, H.; Mešková, M.; Putala, M. *Eur. J. Org. Chem.* **2009**, 3315.

(16) Mešková, M.; Putala, M. *Tetrahedron Lett.* **2011**, *52*, 5379.

(17) (*S*)-**8** was analyzed by ^{1}H and ^{19}F NMR spectroscopy. Because of its high moisture and air sensitivity, it could not be isolated as a pure substance and fully characterized.

(18) Jeulin, S.; de Paule, S. D.; Ratovelomanana-Vidal, V.; Genet, J.-P.; Champion, N.; Dellis, P. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5799.

(19) The absolute configurations of (*S*)-**9**, (*R*)-**9**, and (*R*)-**17**·HCl were determined crystallographically using the effects of anomalous dispersion (see the Supporting Information).

(20) Synthesis of the $-N(i\text{-}Pr)_2$ analogue of (*S*)-**9** was tedious; H_2 activation was slower and irreversible as a result of the amine bulkiness, thus making it less attractive for further studies. The $-N(Me)_2$ analogue of **7** could not be converted into the corresponding aminoborane.

(21) Computational details are provided in the Supporting Information.

(22) The exergonicity of H_2 activation is reduced notably for the conditions used in dehydrogenation experiments ($\Delta G = -5.0$ kcal/mol for $T = 80$ °C and solvent = benzene). It should also be noted that the continuous release of H_2 from the solution shifts the reaction toward H_2 elimination. These nonequilibrium conditions are not taken into account in the present computational approach.

(23) (a) Schwendemann, S.; Tumay, T. A.; Axenov, K. V.; Peuser, I.; Kehr, G.; Fröhlich, R.; Erker, G. *Organometallics* **2010**, *29*, 1067. (b) Stephan, D. W.; Erker, G. *Top. Curr. Chem.* **2013**, *332*, 85.

DOI: 10.1021/ja512658m
J. Am. Chem. Soc. 2015, 137, 4038−4041