JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Communication
pubs.acs.org/JACS

Elusive Metal-Free Primary Amination of Arylboronic Acids: Synthetic Studies and Mechanism by Density Functional Theory

Chen Zhu,[†] Gongqiang Li,[†] Daniel H. Ess,[‡] John R. Falck,[†] and László Kürti*[,†]

[†]Division of Chemistry, Department of Biochemistry, University of Texas Southwestern Medical Center, Dallas, Texas 75390, United States

[‡]Department of Chemistry and Biochemistry, Brigham Young University, Provo, Utah 84602, United States

Supporting Information

ABSTRACT: Herein, we disclose the first *metal-free* synthesis of primary aromatic amines from arylboronic acids, a reaction that has eluded synthetic chemists for decades. This remarkable transformation affords structurally diverse primary arylamines in good chemical yields, including a variety of halogenated primary anilines that often cannot be prepared via transition-metal-catalyzed amination. The reaction is operationally simple, requires only a slight excess of aminating agent, proceeds under neutral or basic conditions, and, importantly, can be scaled up to provide multigram quantities of primary anilines. Density functional calculations reveal that the most likely mechanism involves a facile 1,2-aryl migration and that the presence of an *ortho* nitro group in the aminating agent plays a critical role in lowering the free energy barrier of the 1,2-aryl migration step.

Primary aromatic amines are a prominent class of compounds found in a wide variety of natural products and as key components of pharmaceuticals, agrochemicals, dyes, and polymers.[1] They are most commonly prepared via catalytic hydrogenation or metal-mediated reductions of aromatic nitro compounds,[2] direct substitution of aryl halides with ammonia at high pressure and temperature,[3] and transition-metal (TM)-catalyzed amination of aryl halides with ammonia or its surrogates (Figure 1, A and B).[4] However, these transformations often have several drawbacks, e.g., the concomitant formation of undesired diaryl amines, the use of strong bases, and the requirement for sometimes costly ligands. During the past decade, significant advances have been made in the area of copper-catalyzed oxidative amination of arylboronic acids which offer practical access to a wide variety of *N*-substituted arylamines (e.g., Chan−Lam coupling).[5] More recently, the TM-catalyzed (Pd, Ni, or Cu) electrophilic amination of various organometallic reagents[6] (e.g., Li, Zn, and B) and the direct C−H amination of aromatic rings[7] have received considerable attention for the preparation of *N,N*-dialkylanilines. Surprisingly, the synthesis of primary arylamines from arylboronic acids and derivatives has proven to be far more challenging.[8] For example, Fu et al. only recently achieved the cross-coupling of arylboronic acids with aqueous ammonia in the presence of Cu(I) oxide (Figure 1, C).[8a]

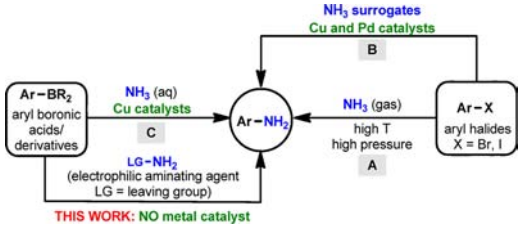
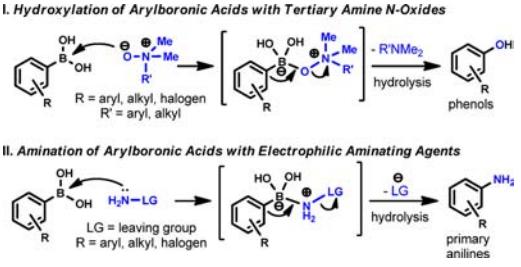


Figure 1. Approaches to primary aromatic amines from aryl halides and aromatic boronic acids/derivatives.

All of the aforementioned achievements are mediated by TMs. From a practical point of view, nonmetal processes are much preferred, especially in the pharmaceutical industry where the removal of undesired metal contamination can be expensive.[9] Moreover, certain functional groups are incompatible with TMs; e.g., the preparation of mono- and polyhalogenated anilines[6e] is often not possible under TM catalysis due to competing cross-coupling processes.

Our recent studies[10] on the hydroxylation of arylboronic acids by *N*-tertiary amine oxides prompted us to investigate if a similar strategy, via a leaving group-initiated 1,2-aryl migration,[11] would also work for the preparation of primary arylamines (Scheme 1).

Scheme 1. Hydroxylation and Amination of Arylboronic Acids via 1,2-Aryl Migration



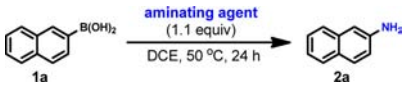
However, it was clear that achieving the metal-free amination would be significantly more challenging, since it is well-known that common electrophilic aminating agents (e.g., hydroxylamine-*O*-sulfonic acid and alkyl azides) do not affect boronic acids and their esters.[12] These aminating agents require the presence of substantially more electrophilic boron derivatives, such as borinic acids, borinic esters, or dichloroboranes.[13] Indeed, a thorough literature search revealed only a handful of

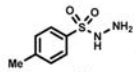
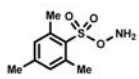
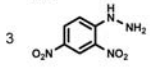
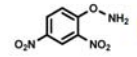
Received: September 28, 2012
Published: October 22, 2012

   dx.doi.org/10.1021/ja309637r | *J. Am. Chem. Soc.* 2012, 134, 18253−18256

recent methods that can convert the C(sp^2)−B bond of arylboronic acids and derivatives to the corresponding C-(sp^2)−N bond in the absence of TMs.[14] For instance, boronic acids can be exchanged for highly electron-deficient nitrogen functional groups (i.e., nitro and nitroso groups) via an aromatic *ipso* substitution mechanism.[14a,d,f] There were also two reports in which electrophilic aminating agents (e.g., organic azides and *N,N*-dialkyl-*O*-benzoylhydroxylamines) reacted with arylboronic acids[14b] and arylboroxines,[14g] respectively, albeit under very harsh reaction conditions (>130 °C), to afford the corresponding *N*-monosubstituted as well as *N,N*-disubstituted anilines. Finally, excess lithiated methoxyamine (3 equiv) was found to aminate arylpinacol boronates, although the scope of this transformation is mostly limited to electron-rich substrates, and base-sensitive functional groups are apparently not compatible with the reaction conditions.[14e] Herein, we disclose a metal-free, mild, operationally simple and practical approach to access primary arylamines by the direct amination of arylboronic acids (Scheme 1, **II**).

Table 1. Potential Aminating Agents for the Conversion of 1a to 2a

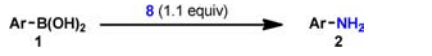


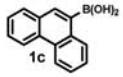
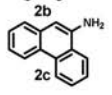
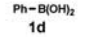
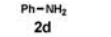
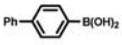
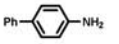
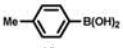
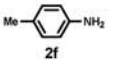
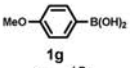
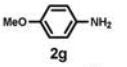
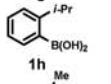
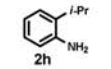
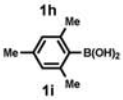
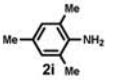
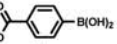
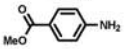
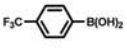
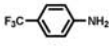
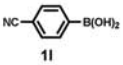
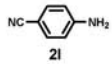
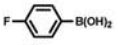
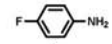
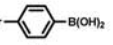
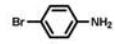
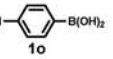
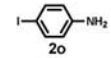
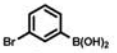
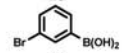
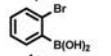
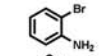
Entry[a]	Aminating Agent		Yield[c] (%)	Entry[a]	Aminating Agent		Yield[c] (%)
1		**3**	0	4[b]		**6**	0
2		**4**	0	5[b]		**7**	0
3		**5**	0	6		**8**	70

[a]Performed on 0.2 mmol scale (0.2 M solution) in DCE. [b]No reaction in other solvents (e.g., toluene, THF, THF:H_2O, dioxane, MeCN, MeOH, DMF) or at temperatures up to 100 °C. [c]Isolated yield.

At the outset, we assessed the reactivity of various potential aminating reagents toward arylboronic acids (Table 1). We hypothesized that the ideal reagent should possess two key structural features: (a) an NH_2 group that is nucleophilic enough to attack the boronic acid and electrophilic enough to accept the migrating aryl group; (b) a weak N−N or N−O bond that upon cleavage facilitates the departure of the leaving group. Attempted amination of 2-naphthylboronic acid (**1a**) with different hydrazine derivatives (**3**−**5**) did not yield the desired primary aryl amine (entries 1−3). Surprisingly, hydroxylamine-*O*-sulfonic acid (HSA, **6**) and *O*-(mesitylenesulfonyl)-hydroxylamine (MSH, **7**), both of which are effective for the conversion of trialkylboranes to alkylamines,[15] also did not transfer the NH_2 group to **1a** (entries 4 and 5). Gratifyingly, the reaction with *O*-(2,4-dinitrophenyl)hydroxylamine (DPH, **8**) furnished the expected primary 2-naphthylamine **2a** in good isolated yield (entry 6). Importantly, aminating reagent **8** is conveniently prepared via Charette's two-step procedure[16] and is stable at 0 °C for several months without appreciable decomposition.[17] With DPH (**8**) selected as the preferred aminating reagent, we next investigated the effect of solvents on the transformation **1a**→**2a**. The choice of solvent was critical for success. Among the examined solvents, only DCE and toluene gave rise to the expected product (**2a**), with the latter resulting in a higher yield (70% vs 76%). Many common solvents such as THF, dioxane, methanol, acetonitrile, DMF, and DMSO were apparently unsuitable for the transformation. At 25 °C, the

Table 2. Scope of Metal-Free Amination Using DPH (8)



Entry[a]	Substrate	T (°C)	Cs_2CO_3 (equiv)	Time (h)	Product	Yield[c] (%)
1	**1a**	50	N/A	24	**2a**	76
2	**1a**	25	1.2	24	**2a**	82
3	 **1b**	50	N/A	24	 **2b**	84
4	 **1c**	50	N/A	24	 **2c**	61
5	 **1d**	50	N/A	24	 **2d**	80
6[b]	 **1e**	50	N/A	24	 **2e**	62
7	 **1f**	50	N/A	20	 **2f**	80
8	 **1g**	50	N/A	4	 **2g**	72
9	 **1h**	50	N/A	48	 **2h**	67
10	 **1i**	25 (DCE)	1.2	48	 **2i**	42
11	 **1j**	100 (THF, sealed tube)	N/A	96	 **2j**	51
12	 **1k**	80	N/A	96	 **2k**	78
13	 **1l**	50 (CH_3CN)	1.2	24	 **2l**	88
14	 **1m**	50	N/A	48	 **2m**	82
15	 **1n**	50	N/A	24	 **2n**	83
16	 **1o**	50 (Dioxane)	N/A	24	 **2o**	60
17	 **1p**	50	N/A	24	 **2p**	54
18	 **1q**	50	N/A	48	 **2q**	66
19	**1r**	50	N/A	96	**2r**	80
20	**1r**	25	1.2	24	**2r**	86
21	**1s**	100	N/A	30	**2s**	56
22	**1t**	100	N/A	72	**2t**	54
23	**1u**	50	1.2	20	**2u**	66

[a]Performed on 0.2 mmol scale (0.2 M solution) in toluene unless shown otherwise. [b]1.5 equiv of reagent **8**. [c]Isolated yield.

dx.doi.org/10.1021/ja309637r | *J. Am. Chem. Soc.* 2012, 134, 18253−18256

amination was slow to complete (>2 d); however, raising the temperature to 50 °C led to the full consumption of **1a** in 24 h.

With the optimized reaction conditions in hand, we turned to explore the scope of substrates (Table 2). Pleasingly, these conditions were compatible with a variety of substituents, regardless of their electronic or steric properties. Toluene as the solvent worked for most substrates; however, in some cases the use of other solvents proved more advantageous (entries 10, 11, 13, and 16). Boronic acids featuring fused aromatic rings furnished the aminated products in good yields (entries 1−4). Generally, the amination of substrates with electron-donating groups (Ph, Me, *i*-Pr, and MeO) resulted in good product yields (entries 6−10). The presence of the strongly electron-withdrawing CF_3, CN, and CO_2Me groups in **1j−l** required extended reaction times (up to 4 days) to reach full conversion (entries 11−13), and in one case the reaction temperature had to be raised to 100 °C. Single or multiple halogen substituents (F, Cl, Br, and I, **1m−t**) at the *ortho*, *meta*, and *para* positions were also well-tolerated in the transformation (entries 14−22). However, polyhalogenated substrates **1s** and **1t** required heating to 100 °C in order to undergo primary amination (entries 21 and 22). The steric bulk of *ortho* substituents also did not prevent the amination of substrates **1h** and **1i** (entries 9 and 10). In the case of the (2,4,6-trimethylphenyl)boronic acid (**1i**) the yield of **2i** was only moderate; however, a single *i*-Pr group in the *ortho* position did not substantially impact the yield of primary aniline **2h** (entry 9). Most substrates could be transformed under mild conditions without any additives. However, in a few special cases, the addition of a base, such as Cs_2CO_3, was beneficial for the reaction. For instance, the base slightly improved the isolated yield of 2-naphthylamine **2a** (entry 2), or significantly shortened the reaction time (24 vs 96 h) and also reduced the required reaction temperature (25 vs 50 °C) for **1r** (entry 20). For unknown reasons, *N*-acyl-substituted boronic acids do not undergo primary amination under the optimized reaction conditions. In addition, substrates containing unprotected nitrogen atoms (e.g., indole, pyrrole), sulfur atoms (e.g., thiophene), and carbonyl groups (e.g., aryl ketones) are not compatible with the reaction conditions. These findings were not very surprising since pyridines and pyrroles are known to undergo *N*-primary amination in the presence of aminating agent **8**.[16] We were pleased to find, however, that an oxygen-containing heteroaromatic boronic acid such as **1u** was smoothly aminated to afford **2u** in good isolated chemical yield (entry 23).

To understand the mechanism and novel reactivity of reagent **8**, we have used the M06-2X density functional method[18] to calculate possible transition states and pathways for reaction with $PhB(OH)_2$. We first examined possible radical pathways since the computed N−O bond dissociation free energy (BDFE) of reagent **8** is relatively small (29.9 kcal/mol). However, all pathways considered result in radical Wheland-type intermediates that have ΔG values greater than ~40 kcal/mol. We explored concerted mechanisms that begin from the B−N dative bond complex (**Complex-8**, Figure 2). From this slightly endergonic complex, the lowest energy concerted pathway involves the 1,2-aryl migration transition state, **TS-1**, that has $\Delta G^{\ddagger}$ = 28.0 kcal/mol relative to separated $PhB(OH)_2$ and **8**.[19] In **TS-1** the Ph−B bond is stretched to 1.75 Å and the Ph−N bond is formed at 2.03 Å. There is also simultaneous N−OAr bond cleavage (1.85 Å) and shortening of the B−N bond (1.52 Å). The product resulting from **TS-1** is the $(PhNH_2)B(OH)_2(OAr)$ complex, which is highly exergonic with ΔG_{rxn} = −72.0 kcal/mol.

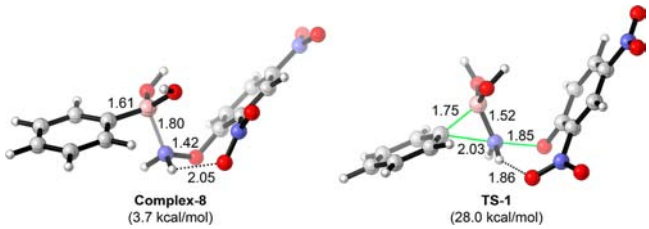


Figure 2. 1,2-Aryl migration transition state. Bond lengths in Å.

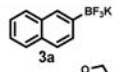
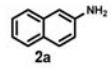
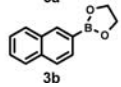
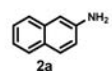
To understand why reagent **8** provides a facile 1,2-migration pathway, we investigated the impact of the NO_2 groups in stabilizing **TS-1**. Removal of only the *p*-NO_2 group increases $\Delta G^{\ddagger}$ by 4.4 kcal/mol. Surprisingly, removal of only the *o*-NO_2 group increases $\Delta G^{\ddagger}$ by 12.2 kcal/mol. This shows that the *o*-NO_2 group is key in providing a low barrier for 1,2-aryl migration because it both stabilizes the developing aryl oxide anion and participates in a H-bonding interaction with one of the amino NH bonds.

In accordance with no product formation, reagents **3**−**5** have $\Delta G^{\ddagger}$ = 54−66 kcal/mol for aryl migration. Reagents **6** and **7** have $\Delta G^{\ddagger}$ = 31.1 and 31.6 kcal/mol, respectively. In general there is a connection between these barrier heights and the N−N and N−O bond strengths of the aminating agents. For reagents **3**, **4**, and **5** the N−N BDFEs are 82.1, 74.1, and 68.4 kcal/mol, respectively. Reagents **6** and **7** with N−O bonds have BDFEs of 52.7 and 49.4 kcal/mol. All of these BDFEs are significantly larger than the N−O BDFE of reagent **8**. However, there is clearly no direct linear correlation between barriers and BDFEs.

We have already established that electron-deficient amination reagents lower the 1,2-aryl migration barrier. To examine the electronic effects of the arylboronic acid, we calculated $\Delta G^{\ddagger}$ values for *para*-substituted versions. This analysis showed that electron-donating groups lower the barrier for migration. This is likely due to facilitating intramolecular attack of the N−O antibond and stabilization of the electron-deficient nitrogen as the anionic OAr group is displaced.

Next, we explored if representative commercially available boronic acid derivatives would also undergo primary amination using **8** (Table 3). To our delight, both 2-naphthyltrifluoroborate

Table 3. Arylboronic Acid Derivatives as Substrates Using Aminating Agent DPH (8)

Entry[a]	Substrate	T (°C)	Cs_2CO_3 (equiv)	Time (h)	Product	Yield[b] (%)
1	 3a	50 (toluene:H_2O = 5:1)	1.2	30	 2a	74
2	 3b	100 (dioxane:H_2O = 5:1)	1.2	24	 2a	73

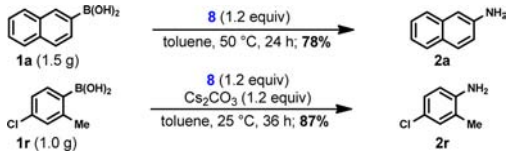
[a]Performed on 0.2 mmol scale (0.2 M solution) in the solvent shown. [b]Isolated yield.

3a and 2-naphthylboronic ester **3b** were converted to the corresponding primary 2-aminonaphthalene **2a** when water was used as a co-solvent in the reaction. In both cases, use of Cs_2CO_3 as an additive improved the isolated yield of **2a**.

Encouraged by the results above, we subsequently conducted the amination reaction on a gram scale, demonstrating its practicality (Scheme 2). When substrates **1a** and **1r** were primary aminated in either the presence or the absence of Cs_2CO_3, the corresponding anilines were obtained in similar chemical yields.

dx.doi.org/10.1021/ja309637r | *J. Am. Chem. Soc.* 2012, 134, 18253−18256

Scheme 2. Primary Amination of Arylboronic Acids on a Gram-Scale Using Aminating Agent DPH (8)



In summary, the first *metal-free amination* of aromatic boronic acids leading to primary arylamines, a reaction that has eluded synthetic chemists for decades, is demonstrated. The transformation is operationally simple, proceeds under mild conditions, and affords structurally diverse primary aniline products in good chemical yield. It is especially noteworthy that a variety of halogenated primary anilines, which often cannot be prepared via the transition-metal-catalyzed amination of the corresponding arylboronic acids and aryl halides, are also readily produced using this method while obviating the formation of undesired *N*-polyarylated products. In addition, the reaction can be readily scaled up to gram scale, thereby offering a practical route for the production of structurally diverse primary arylamines. The exploration of related transformations and several powerful aminating agents is currently under way in our laboratories.

■ ASSOCIATED CONTENT

Supporting Information

Complete experimental procedures and characterization data including ^{1}H and ^{13}C NMR spectra, further computational details, and complete ref 18b. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

laszlo.kurti@utsouthwestern.edu

Notes

The authors declare the following competing financial interest: L.K. and J.R.F. declare a financial interest in Corvinus Chemicals, LLC.

■ ACKNOWLEDGMENTS

L.K. gratefully acknowledges generous financial support from the UT Southwestern Endowed Scholars in Biomedical Research Program (W.W. Caruth, Jr., Endowed Scholarship in Biomedical Research), Robert A. Welch Foundation (Grant I-1764), ACS Petroleum Research Fund (Doctoral New Investigator Grant 51707-DNI1), and American Cancer Society & Simmons Cancer Center Institutional Research Grant (New Investigator Award in Cancer Research, ACS-IRG 02-196). J.R.F. thanks NIH (GM31278) and the Robert A. Welch Foundation (GL-625910) for financial support. D.H.E. thanks BYU and the Fulton Supercomputing Lab for support of this work.

■ REFERENCES

(1) (a) Lawrence, S. A., Ed. *Amines: Synthesis, Properties and Applications*; Cambridge University Press: Cambridge, 2004. (b) Rappoport, Z., Ed. *The Chemistry of Anilines, Parts 1 and 2*; John Wiley & Sons: New York, 2007. (c) Scholz, U.; Schlummer, B. *Sci. Synth.* **2007**, *31b*, 1565. (d) Ricci, A., Ed. *Amino Group Chemistry: From Synthesis to the Life Sciences*; Wiley-VCH: Weinheim, 2008.

(2) (a) Blaser, H. U.; Siegrist, U.; Steiner, H.; Studer, M. *Fine Chem. Heterog. Catal.* **2001**, 389. (b) Mallat, T.; Baiker, A.; Kleist, W.; Koehler, K. *Handb. Heterog. Catal., 2nd ed.***2008**, *7*, 3548. (c) Blaser, H.-U.; Steiner, H.; Studer, M. *ChemCatChem* **2009**, *1*, 210.

(3) Aubin, Y.; Fischmeister, C.; Thomas, C. M.; Renaud, J.-L. *Chem. Soc. Rev.* **2010**, *39*, 4130.

(4) (a) Klinkenberg, J. L.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2011**, *50*, 86. (b) Rao, H.; Fu, H. *Synlett* **2011**, 745.

(5) (a) Qiao, J. X.; Lam, P. Y. S. In *Boronic Acids*, 2nd ed.; Hall, D. G., Ed.; Wiley-VCH: Weinheim, 2011; Vol. *1*, p 315. (b) Qiao, J. X.; Lam, P. Y. S. *Synthesis* **2011**, 829.

(6) (a) Berman, A. M.; Johnson, J. S. *J. Am. Chem. Soc.* **2004**, *126*, 5680. (b) Barker, T. J.; Jarvo, E. R. *J. Am. Chem. Soc.* **2009**, *131*, 15598. (c) Barker, T. J.; Jarvo, E. R. *Synthesis* **2011**, 3954. (d) Olson, D. E. *Mini-Rev. Org. Chem.* **2011**, *8*, 341. (e) Rucker, R. P.; Whittaker, A. M.; Dang, H.; Lalic, G. *Angew. Chem., Int. Ed.* **2012**, *51*, 3953.

(7) (a) Kawano, T.; Hirano, K.; Satoh, T.; Miura, M. *J. Am. Chem. Soc.* **2010**, *132*, 6900. (b) Yoo, E. J.; Ma, S.; Mei, T.-S.; Chan, K. S. L.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 7652.

(8) (a) Rao, H.; Fu, H.; Jiang, Y.; Zhao, Y. *Angew. Chem., Int. Ed.* **2009**, *48*, 1114. (b) Liesen, A. P.; Silva, A. T.; Sousa, J. C.; Menezes, P. H.; Oliveira, R. A. *Tetrahedron Lett.* **2012**, *53*, 4240.

(9) (a) Garrett, C. E.; Prasad, K. *Adv. Synth. Catal.* **2004**, *346*, 889. (b) Welch, C. J.; Albaneze-Walker, J.; Leonard, W. R.; Biba, M.; DaSilva, J.; Henderson, D.; Laing, B.; Mathre, D. J.; Spencer, S.; Bu, X.; Wang, T. *Org. Process Res. Dev.* **2005**, *9*, 198. (c) Qiu, F.; Norwood, D. L. *J. Liq. Chromatogr. Relat. Technol.* **2007**, *30*, 877.

(10) Zhu, C.; Wang, R.; Falck, J. R. *Org. Lett.* **2012**, *14*, 3494.

(11) (a) Jiang, N.; Qu, Z.; Wang, J. *Org. Lett.* **2001**, *3*, 2989. (b) Pei, T.; Chen, C.-y.; Dormer, P. G.; Davies, I. W. *Angew. Chem., Int. Ed.* **2008**, *47*, 4231. (c) Pei, T.; Tellers, D. M.; Streckfuss, E. C.; Chen, C.-Y.; Davies, I. W. *Tetrahedron* **2009**, *65*, 3285.

(12) Hall, D. G. In *Boronic Acids*, 2nd ed.; Hall, D. G., Ed.; Wiley-VCH: Weinheim, 2011; Vol. *1*, p 1.

(13) (a) Brown, H. C.; Heydkamp, W. R.; Breuer, E.; Murphy, W. S. *J. Am. Chem. Soc.* **1964**, *86*, 3565. (b) Rathke, M. W.; Inoue, N.; Varma, K. R.; Brown, H. C. *J. Am. Chem. Soc.* **1966**, *88*, 2870. (c) Brown, H. C.; Kim, K. W.; Cole, T. E.; Singaram, B. *J. Am. Chem. Soc.* **1986**, *108*, 6761. (d) Brown, H. C.; Salunkhe, A. M.; Singaram, B. *J. Org. Chem.* **1991**, *56*, 1170.

(14) (a) Prakash, G. K. S.; Panja, C.; Mathew, T.; Surampudi, V.; Petasis, N. A.; Olah, G. A. *Org. Lett.* **2004**, *6*, 2205. (b) Ou, L.; Shao, J.; Zhang, G.; Yu, Y. *Tetrahedron Lett.* **2011**, *52*, 1430. (c) Wu, X.-F.; Schranck, J.; Neumann, H.; Beller, M. *Chem. Commun.* **2011**, *47*, 12462. (d) Manna, S.; Maity, S.; Rana, S.; Agasti, S.; Maiti, D. *Org. Lett.* **2012**, *14*, 1736. (e) Mlynarski, S. N.; Karns, A. S.; Morken, J. P. *J. Am. Chem. Soc.* **2012**, *134*, 16449. (f) Molander, G. A.; Cavalcanti, L. N. *J. Org. Chem.* **2012**, *77*, 4402. (g) Xiao, Q.; Tian, L.; Tan, R.; Xia, Y.; Qiu, D.; Zhang, Y.; Wang, J. *Org. Lett.* **2012**, *14*, 4230.

(15) Tamura, Y.; Minamikawa, J.; Fujii, S.; Ikeda, M. *Synthesis* **1974**, 196.

(16) Legault, C.; Charette, A. B. *J. Org. Chem.* **2003**, *68*, 7119.

(17) Aminating agent **8** is commericially available from Corvinus Chemicals, LLC in multigram quantities with >99% purity (corvinuschemicals@gmail.com).

(18) (a) All calculations were performed in Gaussian 09 with the M06-2X/6-31G(d,p) functional and basis set in conjunction with the SMD solvent model for toluene. All structures were confirmed as minima or saddle points through normal mode analysis and free energies are reported at 298 K. (b) Frisch, M. J.; et al. *Gaussian 09*, revision A.02; Gaussian, Inc.: Wallingford, CT, 2009. (c) Zhao, Y.; Truhlar, D. G. *Theor. Chem. Acc.* **2008**, *120*, 215. (d) Zhao, Y.; Truhlar, D. G. *Acc. Chem. Res.* **2008**, *41*, 157. (e) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. *J. Phys. Chem. B* **2009**, *113*, 6378.

(19) (a) As a comparison, the $\Delta G^{\ddagger}$ values computed for **TS-1** using the B3LYP, ωB97XD, and BMK functionals with the 6-31G(d,p) basis set are 26.1, 28.7, and 30.2 kcal/mol, respectively. (b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (c) Boese, A. D.; Martin, J. M. L. *J. Chem. Phys.* **2004**, *121*, 3405. (d) Chai, J.-D.; Head-Gordon, M. *Phys. Chem. Chem. Phys.* **2008**, *10*, 6615.