ORGANIC LETTERS

2007
Vol. 9, No. 4
679−681

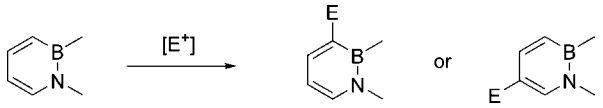
Electrophilic Aromatic Substitution Reactions of 1,2-Dihydro-1,2-azaborines

Jun Pan, Jeff W. Kampf, and Arthur J. Ashe, III*

Department of Chemistry, University of Michigan, Ann Arbor, Michigan 48109-1055
ajashe@umich.edu

Received December 7, 2006

ABSTRACT

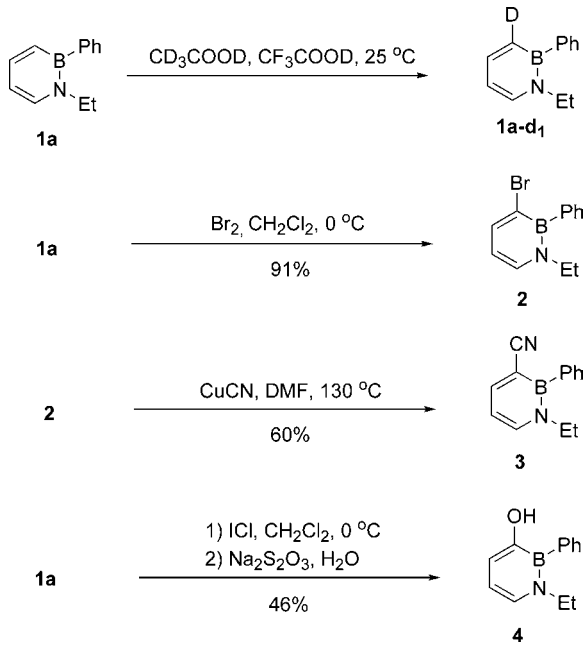


The aromatic boron–nitrogen heterocycle 1,2-dihydro-1,2-azaborine undergoes classical electrophilic substitution. These reactions allow easy functionalization to provide a variety of 3- and 5-substituted derivatives.

Boron−nitrogen heterocycles are becoming increasingly important as ligands[1−4] and for their potential application in organic-based optical and electronic devices.[5] Although these ring systems are moderately easy to prepare, methods for their functionalization are not well developed. For example, the B−N analogue of benzene, 1,2-dihydro-1,2-azaborine **1**, was first prepared in very low yield in 1962,[6] and several ring-fused derivatives of **1** were reported by the Dewar group in the 1960s.[7] However, there has been little further work on the chemistry of the monocyclic system. We recently reported on a good general synthesis of derivatives of **1**[4a] and have reported on their coordination chemistry.[4] We now wish to report that 1,2-dihydro-1,2-azaborines undergo electrophilic aromatic substitution reactions which allow facile functionalization of the ring (Scheme 1).

We initially chose to examine the simplest electrophilic aromatic substitution reaction, acid-catalyzed proton−

Scheme 1



(1) (a) Schmid, G. *Comments Inorg. Chem.* **1985**, *4*, 17. (b) Schmid, G. In *Comprehensive Heterocyclic Chemistry II*; Shinkai, I., Ed.; Pergamon: Oxford, UK, 1996; Vol. 3, p 739.

(2) (a) Ashe, A. J., III; Fang, X. D. *Org. Lett.* **2000**, *2*, 2089. (b) Ashe, A. J., III; Yang, H.; Fang, X. D.; Kampf, J. W. *Organometallics* **2002**, *21*, 4578. (c) Yang, H.; Fang, X. D.; Kampf, J. W.; Ashe, A. J., III. *Polyhedron* **2005**, *24*, 1280. (d) Fang, X. D.; Yang, H.; Kampf, J. W.; Banaszak Holl, M. M.; Ashe, A. J., III. *Organometallics* **2006**, *25*, 513. (e) Pan, J.; Wang, J.; Banaszak Holl, M. M.; Kampf, J. W.; Ashe, A. J., III. *Organometallics* **2006**, *25*, 3463.

(3) (a) Liu, S. Y.; Hills, I. D.; Fu, G. C. *Organometallics* **2002**, *21*, 4323. (b) Liu, S. Y.; Lo, M. M. C.; Fu, G. C. *Angew. Chem., Int. Ed.* **2002**, *41*, 174.

(4) (a) Ashe, A. J., III; Fang, X. D.; Fang, X. G.; Kampf, J. W. *Organometallics* **2001**, *20*, 5413. (b) Pan, J.; Kampf, J. W.; Ashe, A. J., III. *Organometallics* **2004**, *23*, 5626. (c) Pan, J.; Kampf, J. W.; Ashe, A. J., III. *Organometallics* **2006**, *25*, 197.

(5) (a) Sole, S.; Gabbai, F. P. *Chem. Commun.* **2004**, 1284. (b) Wakamiya, A.; Ide, T.; Yamaguchi, S. *J. Am. Chem. Soc.* **2005**, *127*, 14859. (c) Jaska, C. A.; Emslie, D. J. H.; Bosdet, M. J. D.; Piers, W. E.; Sorensen, T. S.; Parvez, M. *J. Am. Chem. Soc.* **2006**, *128*, 10885. (d) Agou, T.; Kobayashi, J.; Kawashima, T. *Org. Lett.* **2006**, *8*, 2241.

(6) (a) Dewar, M. J. S.; Marr, P. A. *J. Am. Chem. Soc.* **1962**, *84*, 3782. (b) Davies, K. M.; Dewar, M. J. S.; Rona, P. *J. Am. Chem. Soc.* **1967**, *89*, 6294. (c) White, D. G. *J. Am. Chem. Soc.* **1963**, *85*, 3634.

(7) For reviews, see: (a) Fritsch, A. J. *Chem. Heterocycl. Compd.* **1977**, *30*, 381. (b) Ander, I. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: Oxford, UK, 1984; Vol. I, p 629.

10.1021/ol062968r CCC: $37.00 © 2007 American Chemical Society
Published on Web 01/24/2007

deuterium isotopic exchange.[8] A large number of data are available for the exchange of aromatic compounds in trifluoroacetic acid. For reasons of compound stability, we have chosen to examine the deuterium exchange of 1-ethyl-1,2-dihydro-2-phenyl-1,2-azaborine (**1a**)[4a] in 1:3 w/w mixtures of trifluoroacetic acid-d_1/ acetic acid-d_4. On mixing **1a** with acid at 25 °C, exchange occurred slowly at C(3)H as indicated by the ^{1}H NMR spectrum. No furthur deuterium exchange was noted. After standing for 24 h at 25 °C, **1a** was converted to phenylboronic anhydride[9] and other unidentified products.

Competition experiments with other heterocycles allowed determination of the relative reactivity. Compound **1a** is more reactive than furan and thiophene but less reactive than 1-methylindole. Compound **1a** is 1.4 times more reactive than 2-methylfuran.[8b] Thus, **1a** is shown to be a highly nucleophilic aromatic compound.

Bromination of **1a** with molecular bromine in CH_2Cl_2 at 0 °C gave a 91% yield of monobromide **2** as a pale yellow oil which slowly crystallized on standing. An X-ray crystal structure of **2** confirmed the assignment as the 3-isomer. The molecular structure of **2** shown in Figure 1 features a C_4-

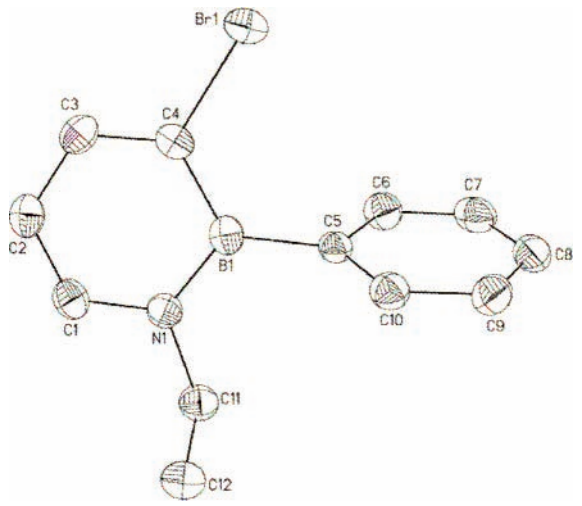


Figure 1. Molecular structure of 3-bromo-1-ethyl-1,2-dihydro-2-phenyl-1,2-azaborine (hydrogen atoms have been omitted for clarity).

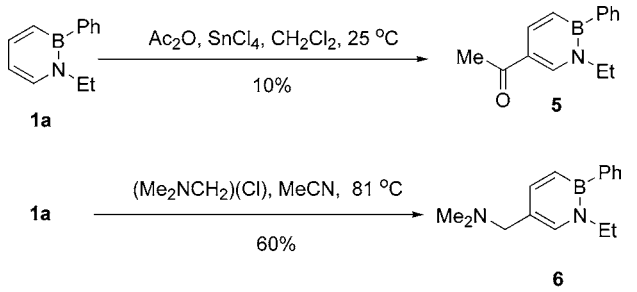
BN-ring which is completely planar. The intraring bond lengths are similar to those previously found for another 2-substituted derivative of **1**[4c] which is consistent with those of an aromatic ring.

Bromide **2** can be converted to nitrile **3** in 60% yield by heating with CuCN in DMF. Although we have not further explored conversions from **2**, it seems likely that the bromide could be converted to other 1,2-dihydro-1,2-azaborine derivatives using the well-honed methods used for the conversion of aryl halides to other aryl derivatives.[10]

The reaction of **1a** with excess iodine monochloride in CH_2Cl_2 at 0 °C followed by quenching with aqueous $Na_2S_2O_3$ gave hydroxy derivative **4** in 46% isolated yield. Although we have not been able to isolate intermediate products, the conversion is consistent with an attack of an iodine electrophile on **1a** followed by a nucleophilic hydrolysis. The IR spectrum of **4** showed bands for a phenolic OH group but none for a carbonyl. Thus, the keto tautomer of **4** is not present in significant concentration. It is plausible to assume that **4** has an aromatic stabilization not present for the keto tautomer.

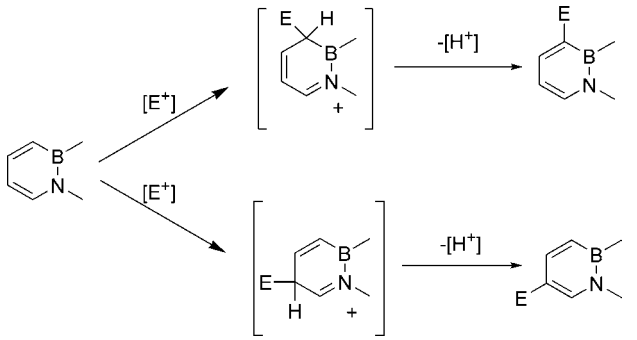
Substitution can also take place at the 5-position (Scheme 2). 1,2-Dihydro-1,2-azaborine **1a** undergoes Friedel−Crafts

Scheme 2



acetylation when treated with acetic anhydride and $SnCl_4$ in CH_2Cl_2 at 25 °C. Unfortunately, the reaction gives a messy product mixture from which the 5-acetyl compound **5** can be isolated in only 10% yield. The Mannich reaction on **1a** is much more successful.[11] Treating **1a** with *N*,*N*-dimethylmethyleneiminium chloride in refluxing acetonitrile gave **6** which could be isolated in 60% yield. No other regioisomers were detected.

Scheme 3



The electrophilic aromatic substitution of **1a** affords either 3- or 5-substituted products depending on the reaction. High-order MO calculations on **1** indicate that the 3- and

(8) (a) Katritzky, A. R.; Taylor, R. *Adv. Heterocycl. Chem.* **1990**, *47*, 1. (b) Salomaa, P.; Kankaanpera, A.; Nikander, E.; Karpainen, K; Aaltonen, R. *Acta Chem. Scand.* **1973**, *27*, 153.

(9) Brock, C. P.; Minton, R. P.; Niedenzu, K. *Acta Crystallogr.* **1987**, *C43*, 1775.

(10) Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400.

5-positions are the most negative[12] and are thus the expected positions for electrophilic attack. Alternatively, resonance stabilization of the putative intermediates for electrophilic substitution as shown in Scheme 3 indicates that attack at the 3- and 5- positions should be favorable.

In conclusion, 1,2-dihydro-1,2-azaborine undergoes the most characteristic aromatic reaction, electrophilic substitution. This reaction allows the preparation of a variety of 3- and 5-substituted derivatives which should greatly facilitate the further exploration of the chemistry of this heterocycle.

Acknowledgment. We thank the National Science Foundation for partial support of this research.

Supporting Information Available: Experimental procedures and compound characterization. X-ray diffraction data for **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL062968R

(11) Heaney, H.; Papageorgiou, G.; Wilkins, R. F. *Tetrahedron Lett.* **1988**, *29*, 2377.

(12) (a) Kranz, M.; Clark, T. *J. Org. Chem.* **1992**, *57*, 5492. (b) Kar, T.; Elmore, D. E.; Scheiner, S. *J. Mol. Struct.* **1997**, *392*, 65.