Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters
Tetrahedron Letters 47 (2006) 7603–7606

Studies on the synthesis of borazines from borane and 1,2-aminoalcohols

Viatcheslav Stepanenko,[a] Margarita Ortiz-Marciales,[a,*] Charles E. Barnes[b] and Carmelo Garcia[a]

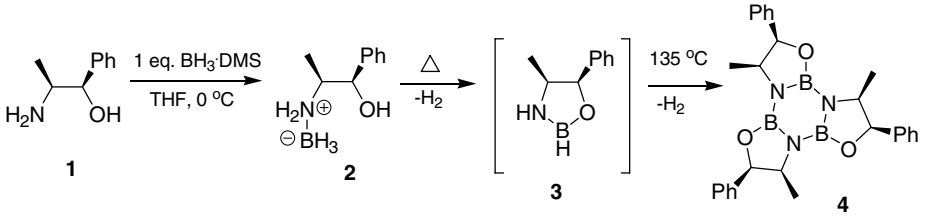
[a]*Department of Chemistry, University of Puerto Rico—Humacao, CUH Station Humacao, PR 00791, USA*
[b]*Department of Chemistry, University of Missouri—Columbia, 125 Chemistry Building, Columbia, MO 65211, USA*

Received 20 July 2006; revised 17 August 2006; accepted 18 August 2006

Abstract—Polycyclic borazines with three adjacent 1,3,2-oxazaborolidine rings were efficiently synthesized by the reaction of 1,2-aminoalcohols or 1,2-aminophenol with borane at room temperature and subsequent cyclization of the intermediate above 120 °C. The X-ray structure of borazine derived from norephedrine indicates an almost planar central aromatic borazine structure condensed with the oxazaborolidine rings and the phenyl and methyl groups at one side of the plane.

Chiral organoborane reagents, in particular 1,3,2-oxazaborolidines, have been extensively studied and applied as efficient Lewis acid catalysts to a wide range of asymmetric transformations.[1,2] B–H oxazaborolidines are commonly used as convenient catalysts for the enantioselective borane reduction of prochiral ketones, imines, and oximes.[1a,c–f,3] The most used method described in the literature for the preparation of B–H oxazaborolidines is by the in situ reaction of chiral aminoalcohols with an excess of borane without isolation and characterization of the catalyst. An alternative method includes the reaction of the aminoalcohol with 1 equiv of borane at 0 °C, followed by heating at 120 °C to give the catalyst.[2a,4] However, there are several reports that unusual side products result, which can influence the enantioselectivity of the reduction.[5] Consequently, detailed studies on the processes involved in the preparation of these often used catalysts are needed in order to prepare more selective catalysts. Herein, we present our studies on the reaction of primary chiral 1,2-aminoalcohols with borane.

In an earlier work, we have attempted to prepare and characterize the B–H oxazaborolidine derived from (1*R*,2*S*)-(−)-norephedrine following reported methods.[4b] However, the ^{1}H NMR of the resulting product was inconsistent with the anticipated structure. Therefore, we decided to explore in detail the different steps of the reaction. When norephedrine reacts with 1 equiv of borane at 0 °C, the *N*-borane complex **2** (Scheme 1) is initially formed, as shown by the ^{1}H and ^{13}C NMR data of the crude reaction mixture.[5e,f] The ^{11}B NMR



Scheme 1. Synthesis of borazine **4** via complex **2**.

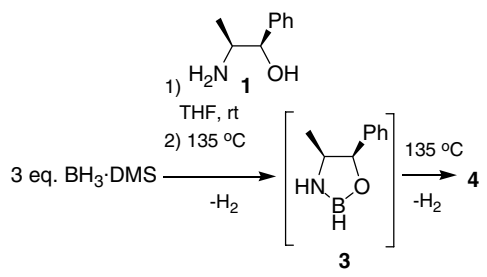
* Corresponding author. Tel.: +1 787 852 3222; fax: +1 787 850 9422; e-mail addresses: mr_ortiz@webmail.uprh.edu; BarnesCh@missouri.edu

0040-4039/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2006.08.071

spectrum shows a signal at −20.6 ppm which, by proton coupling technique appears as an unresolved quartet with $J_{B-H} = 79$ Hz, assigned to the aminoborane complex **2**. After evaporation of the volatiles under vacuum, compound **2** starts to decompose with the evolution of hydrogen at 120 °C. After heating at 135 °C for 1 h, compound **4** was obtained as a colorless glassy material. Although this material was contaminated with some impurities (ca. 15–20%), however, all ^{1}H and ^{13}C NMR signals for the main product are similar to those previously assigned to oxazaborolidine **3**.[4b]

To obtain a better sample, another method was explored. Norephedrine was reacted with an excess of borane at ambient temperature and after the removal of volatiles under vacuum followed by heating at 135 °C for 1 h, borazine **4** was afforded (Scheme 2). In comparison with other similar 1,3,2-oxazaborolidines, the ^{1}H NMR spectrum of the crude product did not have the expected signals of B–H and N–H fragments. The ^{11}B NMR spectrum displays a singlet at 28 ppm attributed to a tri-coordinated boron atom. IR analysis indicates only weak signals characteristic for N–H and B–H bonds. Moreover, the volumetric analysis of hydrogen by hydrolysis of the product indicates the presence of only ca. 5% of active hydride. These data suggest that, under the reaction conditions, the reactive B–H oxazaborolidine **3** undergoes further transformation to the trimeric structure **4** (Scheme 1).

The structure of product **4** was confirmed by HR MS analysis with the signal at 476 (Exp. Mass 476.2491, Calcd. Mass 456.2488) for the molecular ion, less one proton ($(M-H)^{+}$, 100%, $C_{27}H_{29}B_3N_3O_3$). The sample was recrystallized from dry DMSO and the structure of product **4** was conclusively established by X-ray crystallographic diffraction analysis (Fig. 1).[6] In addition, the optimized geometry of the obtained borazine and the electrostatic potential of the molecule were determined by molecular modeling methods using a combination of molecular mechanics, molecular dynamics and quantum theoretical calculations. The bond distance and tensional angles by the more accurate DFT method are in agreement with the experimental X-ray values, as indicated in Table 1. The central part of the molecule, formed by the aromatic borazine ring condensed with three oxazaborolidine rings, is mostly planar with only 3° of deviation, due to the angular tension of the fused five member rings. The methyl and phenyl groups are oriented to one side (cis) of the central planar part of the molecule.



Scheme 2. Synthesis of borazine **4** via reaction of norephedrine with excess of borane.

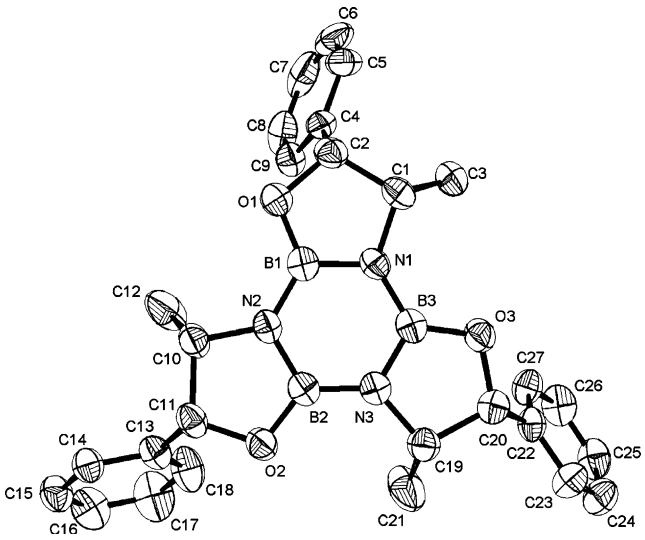


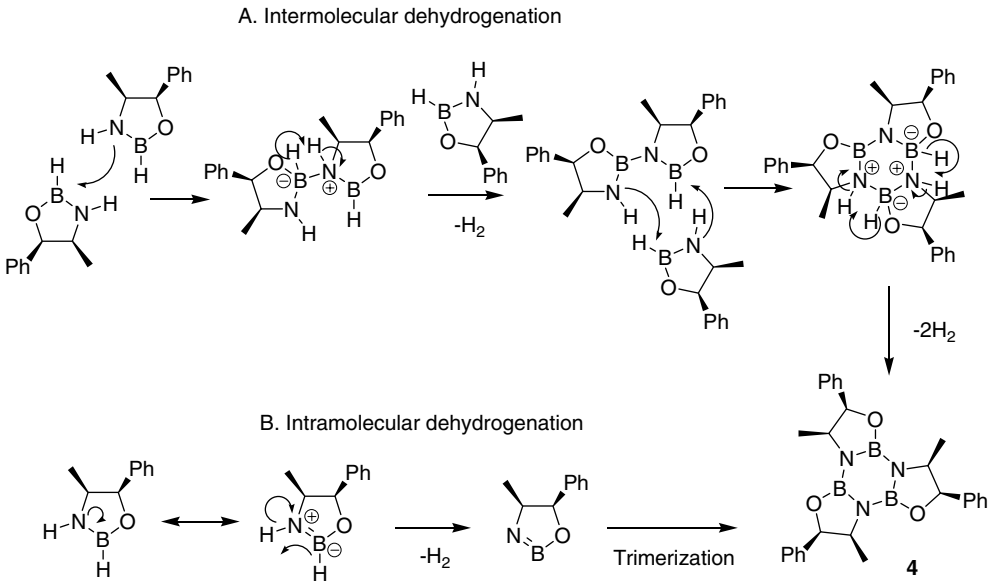
Figure 1. X-ray structure of borazine **4**.

Table 1. Comparative theoretical and experimental molecular parameters of borazine **4**

Parameter	PM3/CI	DFT/B3LYP (6-32G+d)	Crystall. (error values)
B1–N1[a]	1.482	1.440	1.429(3)
B1–N2[a]	1.450	1.424	1.420(3)
B1–O1[a]	1.379	1.379	1.372(3)
B3–N1–B1–O1[b]	160.06	175.48	175.78(17)
N1–B1–N2–B2[b]	19.6	3.8	2.8(3)
O1–C2–C4–C9[b]	−39.8	−35.2	−29.2(3)

[a] Bond distances are in Å.
[b] Torsional angles are in degrees.

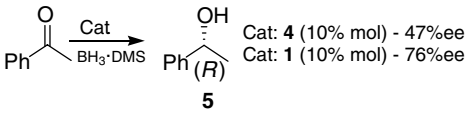
The mechanisms suggested for the formation of the B–N bonds of borazine **4** are shown in Scheme 3. A highly reactive B–H oxazaborolidine **3** is postulated as an intermediate, since under similar conditions, the reaction of the analogous ephedrine (a secondary *N*-methyl 1,2-aminoalcohol) with borane, produced the corresponding B–H oxazaborolidine.[2a,4a,c] Oxazaborolidine **3** can undergo further transformations by one of two pathways: (a) an intermolecular dehydrogenation process of **3** that can form a B–N bond by an initial nucleophilic attack of nitrogen at the electrophilic boron atom followed by the elimination of H_2 and (b) an intramolecular dehydrogenation of the oxazaborolidine can take place to form a 4,5-dihydro-1,3,2-oxazaborole followed by trimerization. We prefer the intermolecular process because the formation of a strained B=N bond in the five member ring is expected to be less favorable. Furthermore, complexes of primary amines with boranes, such as $RBH_2{\cdot}H_2NR^1$, have been well studied and they undergo thermal dehydrocyclization at temperatures above 100 °C to give borazines with general structures like $(RB{-}NR)_3$.[7] Earlier studies of similar reactions have shown that the elimination of hydrogen involves an intermolecular process.[8]



Scheme 3. Possible mechanisms involved in the formation of borazine **4**.

We next examined the catalytic potential of borazine **4** for the asymmetric reduction of acetophenone with borane.[4b] The reduction of acetophenone using 10% of borazine **4** as catalyst (Scheme 4) was sluggish since the reaction mixture contained 20% of starting ketone after 1 h at room temperature. The reaction was completed after 12 h affording 89% isolated yield (R)-(+)-1-phenylethyl alcohol **5**. The enantiomeric purity was 47% ee. Under similar conditions, except that the catalyst was prepared in situ from (1*R*,2*S*)-(−)-norephedrine (10 mol %) with an excess of borane, the reduction was completed within 1 h affording the alcohol in 94% yield and 76% ee.

To demonstrate the generality of the borazine synthesis, chiral borazines **6** and **7** were prepared from (1*R*,2*S*)-(−)-2-amino-1,2-diphenylethanol and (1*R*,2*S*)-(+)-aminoindanol (Fig. 2). The borazine formation of these compounds starts at 120 °C, but require higher temperatures (upto 170 °C) to complete the reaction. These new borazines were also characterized by NMR and HR MS. However, we could not prepare the corresponding borazine from α,α-diphenylvalinol by the same method, but instead, a possible dimeric structure was observed.[5g]



Scheme 4. Asymmetric reduction of acetophenone.

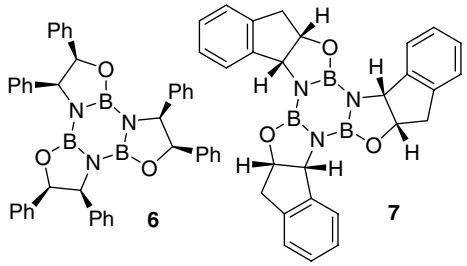
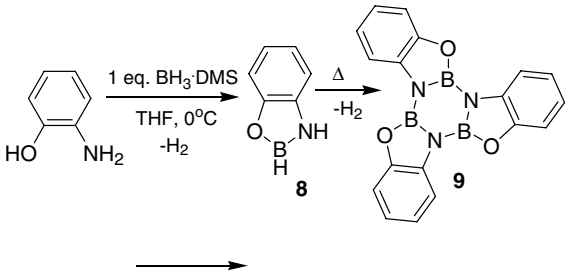


Figure 2. Borazines **6** and **7** derived from (1*R*,2*S*)-(−)-2-amino-1,2-diphenylethanol and from (1*R*,2*S*)-(+)-aminoindanol.

In contrast to aminoalcohols, 2-aminophenol reacts cleanly with 1 equiv of borane at 0 °C to afford an oxazaborolidine derivative **8** (Scheme 5). The ^{11}B NMR spectrum of the reaction mixture exhibits a characteristic doublet at 28 ppm with $J_{B-H} = 172$ Hz. After heating at 120–170 °C and following sublimation at 230 °C, borazine **9** was obtained with 94% yield.

The synthesis of borazines from aminophenoles or aminoalcohols employing BCl_3 or $B(SR)_3$ is known.[9] However, the formation of borazines in the reaction of aminoalcohols and aminophenols with borane has not been reported.

In conclusion, we have found a convenient and facile method to obtain borazines with good purity and in high yield by heating aminoalcohols with borane. Conversely, we do not recommend the use of this method to prepare B–H oxazaborolidines derived from primary chiral 1,2-aminoalcohols as catalysts for asymmetric reductions because the presence of **4** results in lower ee's.



Scheme 5. Reaction of 2-aminophenol with borane.

Acknowledgments

The financial support by the National Institute of Health through their MBRS (GM 08216) and NIH-IMBRE (NC P20 RR-016470) Grants is greatly appreciated. We thank Professor Franklin A. Davis for his help in obtaining the HR MS of borazine **4**, and Professor Bakthan Singaram for insightful discussions.

References and notes

1. For reviews see: (a) Glushkov, V. A.; Tolstikov, A. G. *Russ. Chem. Rev.* **2004**, *73*, 581–608; (b) Corey, E. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 1650–1667; (c) Fache, F.; Schulz, E.; Tomamasino, M.; Lemaire, M. *Chem. Rev.* **2000**, *100*, 2159–2231; (d) Corey, E. J.; Helal, C. J. *Angew. Chem., Int. Ed.* **1998**, *37*, 1986–2012; (e) Deloux, L.; Srebik, M. *Chem. Rev.* **1993**, *93*, 763–784; (f) Singh, V. K. *Synthesis* **1992**, 605–617.
2. For representative examples see: (a) Joshi, N. N.; Srebnik, M.; Brown, H. C. *Tetrahedron Lett.* **1989**, *30*, 5551–5554; (b) Ryu, D. H.; Corey, E. J. *J. Am. Chem. Soc.* **2004**, *126*, 8106–8107; (c) Takasu, M.; Yamomoto, H. *Synlett* **1990**, 194–197; (d) Sartor, D.; Saffrich, J.; Helmchen, G. *Synlett* **1990**, 197–199; (e) Corey, E. J.; Shibata, T.; Lee, T. W. *J. Am. Chem. Soc.* **2002**, *124*, 3808–3809; (f) Berkessel, A.; Mukherjee, S.; Lex, J. *Synlett* **2006**, 41–44; (g) Kinugasa, M.; Harada, T.; Oku, A. *Tetrahedron Lett.* **1998**, *39*, 4529–4532; (h) Kinugasa, M.; Harada, T.; Oku, A. *Tetrahedron Lett.* **1998**, *39*, 5535–5536; (i) Bringmann, G.; Hartung, T. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 761; (j) Kiyooka, S.; Kaneko, Y.; Komura, M.; Matsuo, H.; Nakano, M. *J. Org. Chem.* **1991**, *65*, 2276–2278.
3. (a) Itsuno, S.; Nakano, M.; Miyazaki, K.; Masuda, H.; Ito, K. *J. Chem. Soc., Perkin Trans. 1* **1885**, 2039–2044; (b) Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551–5553; (c) Itsuno, S.; Sakurai, Y.; Shimizu, K.; Ito, K. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1859–1863; (d) Cho, B. T.; Ryu, M. h. *Bull. Korean Chem. Soc.* **1994**, *15*, 191; (e) Quallich, G. J.; Keavey, K. N.; Woodall, T. M. *Tetrahedron Lett.* **1995**, *36*, 4729–4732; (f) Yadav, J. S.; Reddy, P. T.; Hashim, S. R. *Synlett* **2000**, *7*, 1049–1051; (g) Fontaine, E.; Namane, C.; Meneyrol, J.; Geslin, M.; Serva, L.; Royssey, E.; Tissandie, S.; Maftouh, M.; Roger, P. *Tetrahedron: Asymmetry* **2001**, *12*, 2185–2189; (h) Krzeminski, M. P.; Zaildewiccz, M. *Tetrahedron: Asymmetry* **2003**, *14*, 1463–1466.
4. (a) Brown, J. M.; Lloyd-Jones, G. C. *Tetrahedron: Asymmetry* **1990**, *1*, 865–868; (b) Quallich, G. J. U.S. Patent 6037505, 2000; (c) Ortiz-Marciales, M.; González, E.; Figueroa, R.; De Jesús, M.; Martínez, J.; Espinosa, S.; Correa, W. *Organic Lett.* **2003**, *5*, 3447–3449.
5. (a) Brown, J. M.; Guy, C.; Lloyd-Jones, G. C.; Layzell, T. P. *Tetrahedron: Asymmetry* **1993**, *4*, 2151–2154; (b) Lang, A.; Noth, H.; Schmidt, M. *Chem. Ber.* **1997**, *130*, 241–246; (c) Mathre, D. J.; Thompson, A. S.; Douglas, A. W.; Carroll, J. D.; Corley, E. G.; Grabowski, E. J. J. *J. Org. Chem.* **1993**, *58*, 2880–2888; (d) Ortiz-Marciales, M.; De Jesus, M.; Gonzales, E.; Raptis, R. G.; Baran, P. *Acta Crystallogr., Sect. C* **2004**, *60*, 173–175; (e) Tlahuext, H.; Santiesteban, F.; García-Báez, E.; Contreras, R. *Tetrahedron: Asymmetry* **1994**, *5*, 1579–1588; (f) Santiesteban, F.; Mancilla, T.; Klaébe, A.; Contreras, R. *Tetrahedron Lett.* **1983**, *24*, 759–760; (g) Brunel, J. M.; Maffei, M.; Buono, G. *Tetrahedron: Asymmetry* **1993**, *4*, 2255–2260.
6. The crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the Deposition Number CCDC 288342.
7. Niedenzu, K.; Dawson, K. J. *Boron–Nitrogen Compounds*; Academic Press: New York, 1965.
8. (a) Ryschkewictsch, G. E.; Willings, J. W. *Inorg. Chem.* **1970**, *9*, 314; (b) Jaska, C. A.; Temple, K.; Lough, A. J.; Manners, I. *J. Am. Chem. Soc.* **2003**, *125*, 9424–9434.
9. (a) Rudner, B.; Harris, J. J. U.S. Patent 3 100 791, 1959; (b) Brotherton, R. J.; Steinberg, H. J. *J. Org. Chem.* **1961**, *26*, 4632–4634; (c) Harris, J. J.; Rudner, B. *J. Org. Chem.* **1962**, *27*, 3848–3851; (d) Cragg, R. H.; Weston, A. F. *J. Chem. Soc., Chem. Commun.* **1972**, 79–80; (e) Cragg, R. H.; Weston, A. F. *J. Chem. Soc., Dalton Trans.* **1975**, 93–95; (f) Cragg, R. H.; Weston, A. F. *J. Chem. Soc., Dalton Trans.* **1975**, 1761–1764.