Ruthenium-Catalyzed Tandem Activation of C≡N and B–H Bonds under Dihydrogen: Synthesis of BN Heterocycles

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Ruthenium-Catalyzed Tandem Activation of C≡N *and* B-H Bonds under Dihydrogen: Synthesis of BN Heterocycles.

Marion Beguerie,[a] Charly Faradji,[a] Laure Vendier,[a] Sylviane Sabo-Etienne,[a] and Gilles Alcaraz,*[b]

Dedication ((optional))

Abstract: The incorporation of a nitrile function ortho to the B(sp^2)HN^{i}Pr$_2$ group to obtain cyano(aryl)boranes and their subsequent ruthenium catalyzed transformation under dihydrogen atmosphere (1 bar) provides a direct access to NH-containing 1*H*-2,1-benzazaboroles as BN-analogues of indene, in very mild conditions (RT). The BN-heterocycle can be functionalized from the corresponding lithium amide either by N-elementation with various p-block (C, Si, P, B) electrophiles or by palladium catalyzed N-arylation with aryl bromides, affording a new and powerful protocol for B-N bond decoration.

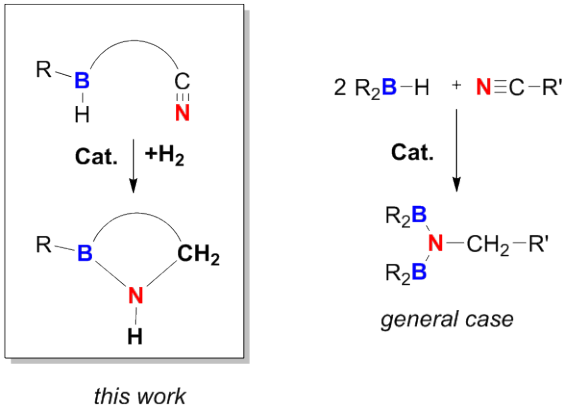
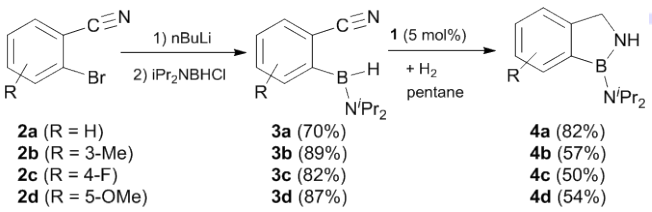


Figure 1. N(sp^2)-B(sp^2) bond formation from nitriles and boranes.

The development of clean and selective methods for the reduction of a nitrile function remains a major challenge in organic chemistry.[1] A number of approaches have been proposed to reduce the C≡N triple bond. They involve metal hydrides in stoichiometric amounts,[2] catalyzed hydrogenation[3] or hydrosilylation.[4] More recently, catalyzed hydroboration[5] of nitriles has received increasing attention and the reduction can be achieved with boranes of moderate Lewis acidity, under relatively mild conditions, leading specifically to the geminal aminodiboryl compounds (Figure 1). Little attention is generally paid to the newly formed N–B bonds, and the corresponding amine is commonly obtained by protolytic deprotective workup along with the boron-containing waste.

Based on our previous studies on catalyzed dehydrogenative cyclization of amine-boranes[6] and nitrile hydrogenation,[3c] we reasoned that incorporating a reductive nitrile function ortho to the B–H bond, could open new synthetic strategies to BN-embedded heterocycles[7] through catalyzed C≡N and B–H activation pathways. Herein, we report the synthesis of cyano mono-boranes and their transformation into N-unsubstituted 1*H*-2,1-benzazaboroles by a catalyzed process using the ruthenium complex [RuH$_2$(η^2-H$_2$)$_2$(PCy$_3$)$_2$] (**1**) as a catalyst precursor under dihydrogen atmosphere. Subsequent reactivity studies highlight the potential for further functionalization by furnishing a variety of BN molecules upon reaction with electrophiles as well as through Buchwald-Hartwig amination.

The reaction sequence was first established with the representative 2-cyanophenyl(amino)borane **3a** possessing a nitrile group ortho to the B(sp^2)–H borane function. **3a** was prepared in 70% isolated yield via a lithiation/borylation sequence from 2-bromobenzonitrile **2a** and HClBN^{i}Pr$_2$ according to the procedure previously reported for the synthesis of phosphino~boranes (Scheme 1).[8]



2a (R = H) **3a** (70%) **4a** (82%)
2b (R = 3-Me) **3b** (89%) **4b** (57%)
2c (R = 4-F) **3c** (82%) **4c** (50%)
2d (R = 5-OMe) **3d** (87%) **4d** (54%)

Scheme 1. Synthesis of 2-cyanophenyl(amino)boranes **3** and 1*H*-2,1-benzazaboroles **4**.

Compound **3a** is stable at room temperature and was fully characterized by multinuclear NMR. A doublet at δ 37.5 ($^1J_{BH}$ = 115 Hz) and a broad singlet at δ 5.52 in the ^{11}B NMR and ^{1}H{^{11}B} NMR spectra,[8a, 8d] respectively, reflect the presence of a B(sp^2)HN^{i}Pr$_2$ group in **3a**. The integrity of the cyano group is evidenced by a strong nitrile IR stretching frequency observed at 2219 cm^{-1}. The identity of **3a** was unambiguously confirmed by X-ray diffraction techniques (Figure 2). The reaction of **3a** in pentane, at room temperature, in the presence of a catalytic amount of **1** (5 mol%) under dihydrogen (1 bar), led to the complete disappearance of **3a** after 5h as monitored by ^{1}H and ^{11}B NMR. The formation of a new compound exhibiting a singlet at δ 30.6 in the ^{11}B NMR was observed whereas no signal around δ 5.5 in the ^{1}H{^{11}B} NMR spectrum was detected. The infrared spectrum showed the complete disappearance of the nitrile band and the presence of a new band at 3480 cm^{-1} in the NH region. Compound **4a** was isolated as a white solid in 82%

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yield (Scheme 1) and was fully characterized by NMR spectroscopy and X-ray crystallography (Figure 2).

4a formally results from the reduction of the nitrile function and the activation of the B–H bond leading for the first time to the formation of the cyclic 1*H*-2,1-benzazaborole featuring a NH group. The reaction is catalyzed under dihydrogen atmosphere and it is noteworthy that no 1,1-bis(boryl)amine oligomers formally resulting from a double B–H insertion[5a-f] were detected. The scope of the reaction was extended to 2-cyanophenyl(amino)boranes displaying different arene substitution patterns. The reactions remained clean when monitored by NMR spectroscopy and the substituted cyclized compounds **4b-d** could also be obtained and isolated in good yields as rare examples of 1*H*-2,1-benzazaboroles.[9]

As a BN-indene derivative, **4a** presents an ortho-fused bicyclic planar structure. The exocyclic nitrogen atom (N2) adopts a trigonal planar geometry as evidenced by the sum of the C8-N2-B, C11-N2-B and C8-N2-C11 angles (ΣN2 = 360.01°). The N1–B (1.4317(18) Å) and N2–B (1.4120(16) Å) bond distances are indicative of significant conjugation between the nitrogen atoms (N1 and N2) and the boron.[10] The exocyclic N2–B is significantly elongated by comparison to **3a** (N2–B (1.3830(14) Å) whereas the intracyclic N1–B is slightly elongated by comparison to a substituted alkyl benzazaborole as reported by Dostal.[9f] The B1–C1 bond length (1.5907(19) Å) is comparable to the one in compound **3a** and falls within the range of a single B–C bond as compared with the sum of the covalent radii (1.6 Å).[11]

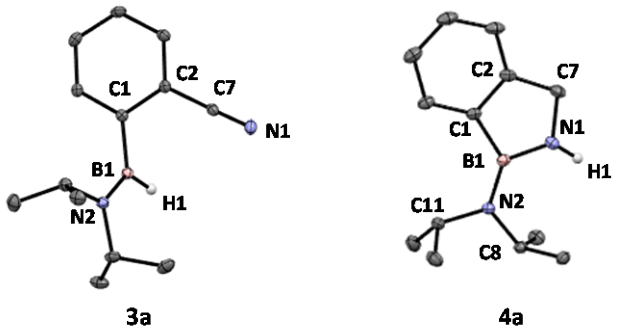


Figure 2. X-ray structure of cyanophenyl(amino)borane **3a** (left) and 1*H*,2-1-benzazaborole **4a** (right). The hydrogens associated with the carbon atoms are omitted for clarity. Ellipsoids are shown at 30% probability.

We were then interested in the chemical behavior of 1*H*-benzazaborole **4** under basic conditions and more particularly in the reactivity of the B-NH-CH_2 grouping. The reaction was conducted with **4a** in ether, at –20°C, by adding a stoichiometric amount of butyllithium and led to the rapid formation of lithium boramidinate salt **5** as an insoluble and stable white precipitate. After workup, **5** was isolated (76%) and fully characterized by multinuclear NMR and infrared spectroscopy. In the ^{11}B NMR, the relatively deshielded signal at δ 38 is indicative of the presence of a B(sp^2)N moiety excluding any quaternized boron atom.[9i] The X-ray structure was determined at 110K confirming the identity of **5**. As illustrated in Figure 3, the asymmetric unit contains two independent lithium boramidinates associated in a pattern with the 1*H*-benzazaborole backbones in two nearly perpendicular planes (ca 82°). This pattern adopts a head-to-tail arrangement forming a centrosymmetric ladder-type structure. Each lithium is in a three-coordinate environment having a close contact with three 1*H*-2,1-benzazaborole endocyclic nitrogens for Li1, and only two in the case of Li2 that is additionally connected to one N^{i}Pr$_2$ nitrogen atom.

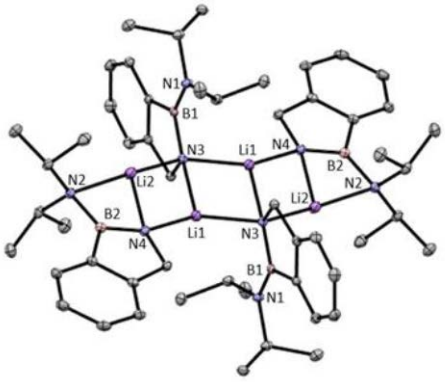
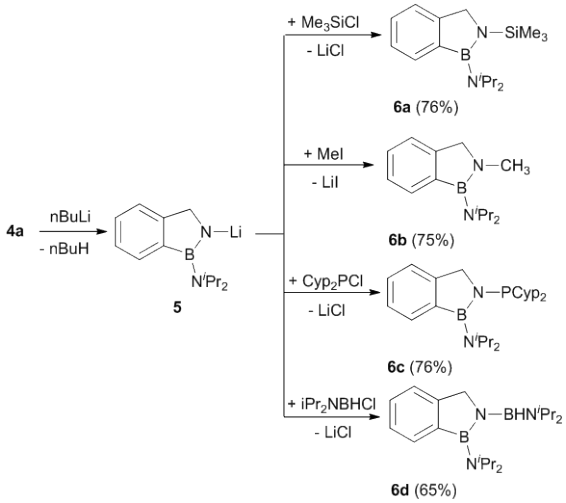


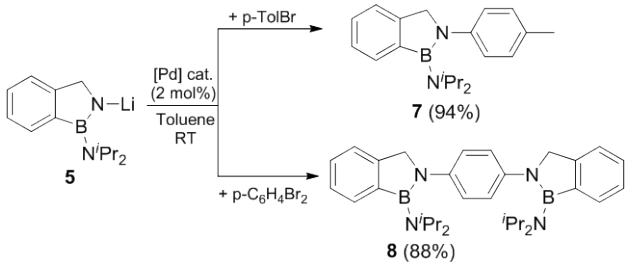
Figure 3. X-ray structure of lithium boramidinate **5** in ladder-type arrangement. The hydrogens associated with the carbon atoms are omitted for clarity. Ellipsoids are shown at 30% probability.

In a second stage, the synthetic scope of **5** was evaluated via N–E functionalization strategy to introduce various main-group element moieties. The reactions were carried out by generating **5** in situ from **4a** with a palette of electrophilic halides E–X (E = C, Si, B, P) (scheme 2). The corresponding N-substituted 1*H*-2,1-benzazaboroles **6** were obtained in very good overall isolated yields and fully characterized by multinuclear NMR and also by X-ray crystallography in the case of **6b** and **6d** (Sup. Info).



Scheme 2. Synthesis of N-substituted1*H*-2,1-benzazaboroles **6** from **4**.

Going one step further, we envisioned to extend this synthetic methodology for the efficient introduction of aryl groups onto the 1*H*-2,1-benzazaborole core by using **5** in a Buchwald-Hartwig amination.[12] The reaction was performed in dry toluene, at room temperature, with a stoichiometric amount of **5** and aryl halides in the presence of PEPPSITM-IPr (2 mol%) as the palladium precatalyst.[13] The corresponding N-aryl functionalized 1*H*-2,1-benzazaboroles were successfully obtained and spectroscopically characterized. 4-bromotoluene and 1,4-dibromobenzene undergo single and double coupling, leading to 1H-2,1-benzazaborole **7** (94%) and **8** (88%) in excellent isolated yields, respectively (scheme 3). To the best of our knowledge, there are no reports on catalyzed N-arylation of a BN bond. In this prospect, Buchwald-Hartwig amination represents a valuable strategy for the synthesis of late-stage functionalized BN-heterocycles.[14]



Scheme 3. Buchwald-Hartwig amination of aryl halides with **5**.

In conclusion, we have developed a new strategy for the synthesis of BN heterocycles. For the first time, 1*H*-2,1-benzazaboroles **4** displaying an endocyclic NH moiety were prepared starting from a borane featuring a nitrile function. The first step is based on the synthesis of a series of 2-cyanophenyl(amino)boranes **3**. Their subsequent catalyzed transformation involves both B–H and C≡N activation and was cleanly achieved by using the bis(dihydrogen) ruthenium complex **1** as precatalyst under a reductive atmosphere of dihydrogen. Moreover, the potential for broad functionalization of this family of molecules has been assessed starting from the stable lithium amide **5** readily obtained by simple deprotonation of **4** with butyllithium. The introduction of a variety of main-group element moieties at the nitrogen was performed by reaction with electrophiles E-X (E = C, B, Si, P). We also disclose a Buchwald-Hartwig amination protocol enabling the efficient installation of aryl groups at the nitrogen atom from **5**. This N-arylation method should broaden the scope of B–N bond engineering and open the access to more sophisticated BN-embedded molecules and materials. We are currently exploring this field and conducting in-depth studies to understand the mechanism of this novel catalyzed transformation.

CCDC 1535263 (**3a**), 1535264 (**4a**) and 1535265 (**5**), 1535266 (**6b**) and 1535267 (**6d**) contain the supplementary crystallographic data for this paper.

These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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Keywords: Boranes • Catalysis • BN Heterocycles • Hydrogenation • Ruthenium

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