

Synthesis of Boriranes by Double Hydroboration Reactions of N-Heterocyclic Carbene Boranes and Dimethyl Acetylenedicarboxylate

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S Supporting Information

ABSTRACT: Reaction of *bis*-(2,6-diisopropylphenyl)-imidazol-2-ylidene borane with dimethyl acetylenedicarboxylate gives 80% yield of a stable borirane (boracyclopropane) formed by formal double hydroboration along with 5% of the (*E*)-alkenylborane. DFT calculations suggest a mechanism where divergence to the two products occurs after a common initial stage of hydride transfer from the NHC-borane to the acetylenedicarboxylate.

Nuclear analogs of cyclopropanes are common for the elements nitrogen (called azacyclopropanes or aziridines) and oxygen (called oxacyclopropanes, oxiranes or commonly epoxides).¹ Likewise, silicon analogs (silacyclopropanes) are often readily available and have a rich chemistry.² In contrast, boron analogs of cyclopropanes (boracyclopropanes, or hereafter, boriranes) are more rare,³ presumably because they combine two features, ring strain and Lewis acidity, that often impart reactivity (Figure 1).

The Lewis acidity of trivalent boranes can be suppressed by Lewis bases that bind strongly, resisting exchange or displacement.⁴ Thus, Lewis bases can stabilize boriranes. In early work, Denmark made two boriranes tightly complexed to substituted pyridines.⁵ N-Heterocyclic carbenes bind to borane (BH₃) more tightly than pyridines,⁶ and recently Braunschweig^{3,7} and Wang⁷ have made several stable NHC-substituted boriranes.

Like many syntheses of cyclopropanes and other three-membered rings, extant syntheses of boriranes start from alkenes and provide a driving force to account for ring strain in the products. Denmark and Wang used photons to drive their reactions while Braunschweig used the displacement of good leaving groups. For example, reaction of stilbene **1** with elemental sodium provides a disodium stilbene dianion **2**, which in turn reacts with NHC-phenyl dichloroborane **3** to provide NHC-phenylborirane **4** in 53% yield (Scheme 1).³

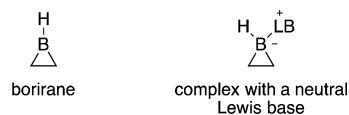


Figure 1. Free and complexed boriranes (boracyclopropanes).

Scheme 1. Reactive Stilbene Dianion and Two Chloride Leaving Groups Enable the Synthesis of Stable NHC-Borirane **4**

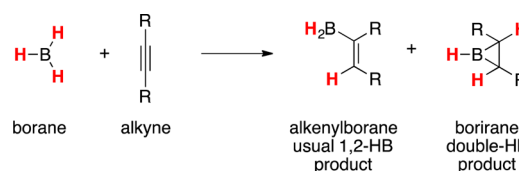
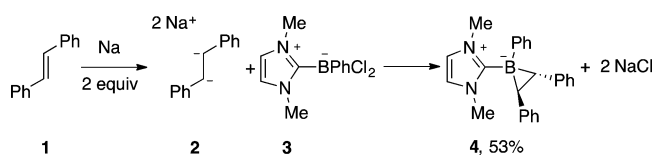


Figure 2. Hypothetical double hydroboration of an alkyne to make a borirane, an unknown reaction.

Different mechanisms have been suggested for this kind of reaction,^{3a,8} but in any case the formation of 2 equiv of NaCl is an important driving force.

Here we report a direct synthesis of NHC-boriranes by reactions of acetylenedicarboxylate esters with NHC-boranes. The reaction is simply a net double hydroboration (Figure 2). Hydroborations of alkynes typically give alkenylboranes.⁹ To the best of our knowledge, this is the first example of hydroboration of an alkyne to give a Lewis base-stabilized borirane.¹⁰

Most alkynes resist uncatalyzed hydroboration by NHC-boranes.¹¹ In contrast, arynes are rapidly hydroborated by NHC-boranes, presumably due to their strain and electrophilicity.¹² NHC-boranes are good hydride donors,¹³ so we hypothesized that they might hydroborate electron poor alkynes like acetylenedicarboxylates by a hydride transfer pathway.

Indeed, 1,3-dimethylimidazol-2-ylidene borane **5a** (1 equiv) and dimethyl but-2-ynedioate **6** (dimethyl acetylenedicarboxylate, 2 equiv) reacted in THF at rt to give two new NHC-borane products in a 33/67 ratio according to ¹¹B NMR spectroscopic analysis (Table 1). However, heat was evolved

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Table 1. Results of Hydroboration Reactions of Dimethyl Acetylenedicarboxylate 6 by NHC-Boranes

5a, R = Me
b, R = iPr
c, R = Mes
d, R = dipp

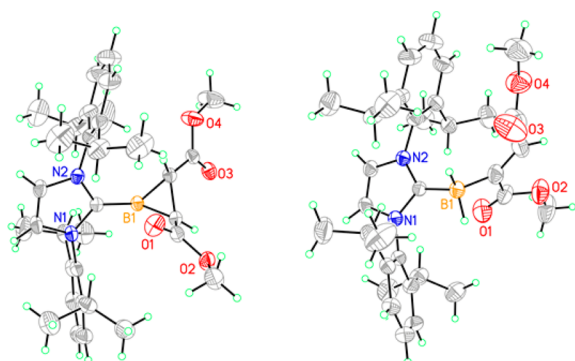
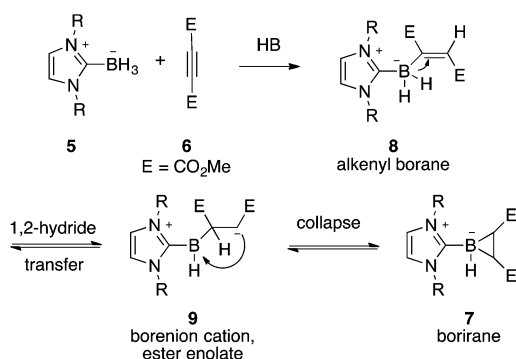
6
2 equiv

conditions
a, THF, -78 °C to rt, 18 h
b, THF, -78 °C to rt, 18 h
c, MeCN, 80 °C, 1 h
d, MeCN, 80 °C, 18 h

7a-d
8a-d

entry	NHC-borane	ratio 7/8 ^a	yield 7 ^b	yield 8 ^b
a	5a, R = Me	33/67	19%	35%
b	5b, R = iPr	52/48	14%	29%
c	5c, R = Mes ^c	81/19	31%	10%
d	5d, R = dipp ^d	86/14	80%	5%

^aFrom integration of the ¹¹B NMR spectrum of the reaction mixture; ^bIsolated by flash chromatography; ^cMes is mesityl (2,4,6-trimethylphenyl); ^ddipp is 2,6-diisopropylphenyl

**Figure 3.** Crystal structures of borirane 7d (left) and (E)-alkenylborane 8d (right).**Figure 4.** Sensible path to 7 based on hydroboration, 1,2-hydride shift and collapse is not occurring because control experiments show that 7 and 8 do not interconvert.

and a significant amount NHC-borane remained unreacted, suggesting that oligomerization of 6 was competing. To minimize the dicarboxylate side reaction, 5a and 6 were mixed at -78 °C, then allowed to warm slowly to rt and stirred overnight. In this reaction (Table 1, entry a), 95% of the NHC-borane 5a was converted to the same two products, again 33/

67 ratio. The THF was removed and the residue was purified by automated flash chromatography.

The major product was isolated in 35% yield and exhibited a triplet at -28.2 ppm ($J = 85.6$ Hz) in its ¹¹B NMR spectrum. The ¹H and ¹³C NMR spectra identified this as (E)-alkenylborane 8a, already an interesting product because uncatalyzed *trans*-hydroboration reactions are rare.¹⁴

The minor product was isolated in 19% yield and proved even more interesting. This exhibited a doublet in the ¹¹B NMR spectrum, suggesting that it might simply be the product of hydroboration of an 8a by second molecule of alkyne 6 to give a dialkenylborane. However, the chemical shift (-26.6 ppm) seemed too far upfield and the J_{BH} value (123.3 Hz) was also unusual. Such a large value suggested that the minor product might be borirane 7a.

The ¹H and ¹³C NMR spectra confirmed the borirane structure. The two borirane hydrogen atoms in 7a appear as broad upfield resonances at 1.58 and 1.06 ppm in the ¹H NMR spectrum. The borirane carbon resonances are broad and weak (typical for carbons bonded to boron), but can be located upfield at 26.80 and 24.95 ppm in the ¹³C NMR spectrum. These data also show that the two ester groups are configured *trans* on the borirane ring. HRMS analysis confirmed that both 7a and 8a are 1/1 adducts of 5a and 6.

Reaction of 1,3-diisopropylimidazol-2-ylidene borane 5b with 6 under the same conditions (Table 1, entry b) gave a 52/48 mixture of products 7b and 8b, which were isolated in 14% and 29% yield. The structures, borirane for 7b and (E)-alkenylborane for 8b, were clear from the NMR spectra.

Increased amounts of boriranes were obtained from *N*-aryl substituted NHC-boranes. The dimesityl NHC-borane 5c did not react readily with 6 at rt in THF. However, reaction in refluxing acetonitrile was complete in 1 h and now provided the borirane 7c as the major product (7c/8c ratio, 81/19). The isolated yields of borirane 7c and the (E)-alkenylborane 8c were 31% and 10%, respectively (Table 1, entry c).

The best results were obtained with *bis*-(2,6-diisopropylphenyl)imidazol-2-ylidene borane 5d. This gave high conversion after 18 h in refluxing acetonitrile, and the ratio of borirane 7d to (E)-alkenylborane 8d was 86/14 (Table 1, entry d). These products were separated by flash chromatography to give 7d in 80% yield and 8d in 5% yield. This reaction was scaled up to provide over 1 g of borirane 7d, which is a stable white solid, mp 225–227 °C.

Crystal structures of both dipp NHC-borane products 7d and 8d were solved and are shown in Figure 3. (The crystal structures of boriranes 7b and 7c and alkenylborane 8c are shown in the SI.)

The esters of borirane 7d are *trans*-configured, as deduced from the ¹H NMR spectrum. The BH bond and the two CH bonds of the borirane ring are rather short, 1.092, 0.991, and 0.984 Å, respectively. The internal bond angles of the borirane ring are close to ideal; 61.46° and 61.58° for the two B–C–C angles, and 56.96° for the C–B–C angle. On the other hand, the dihedral angles of the C–C bond of the borirane are rather open: 146.4° for HCCH and 136.6° for C_{ester}CCC_{ester}. In classical resonance terms, the borirane might have slight character of a complex between a borylene (NHC-BH:) and an alkene (dimethyl fumarate).

Alkenyl NHC-borane 8d is the E-isomer resulting from net *trans*-1,2-hydroboration. Alkenylboranes 8a–c exhibit similar spectra to 8d, so they are also E-isomers.

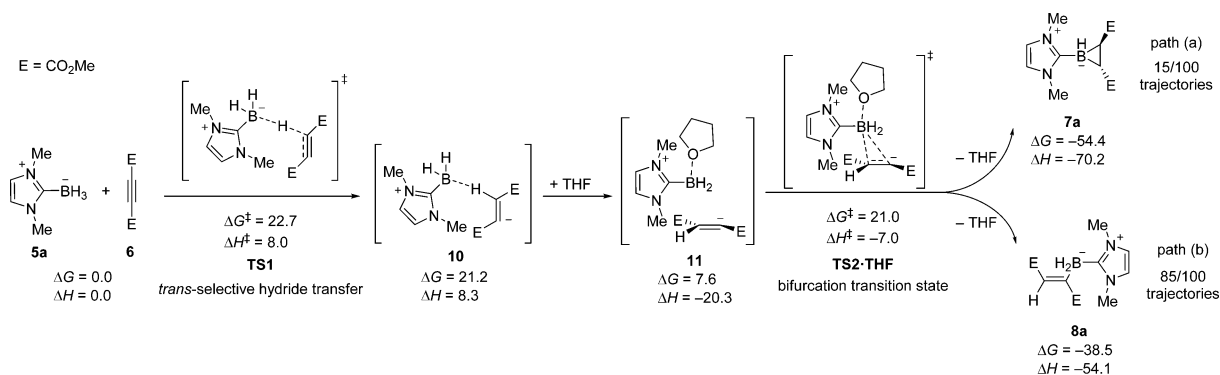


Figure 5. Mechanisms of the formation of borirane and alkenylborane. All energies are in kcal mol^{-1} and with respect to **5a** and **6**.

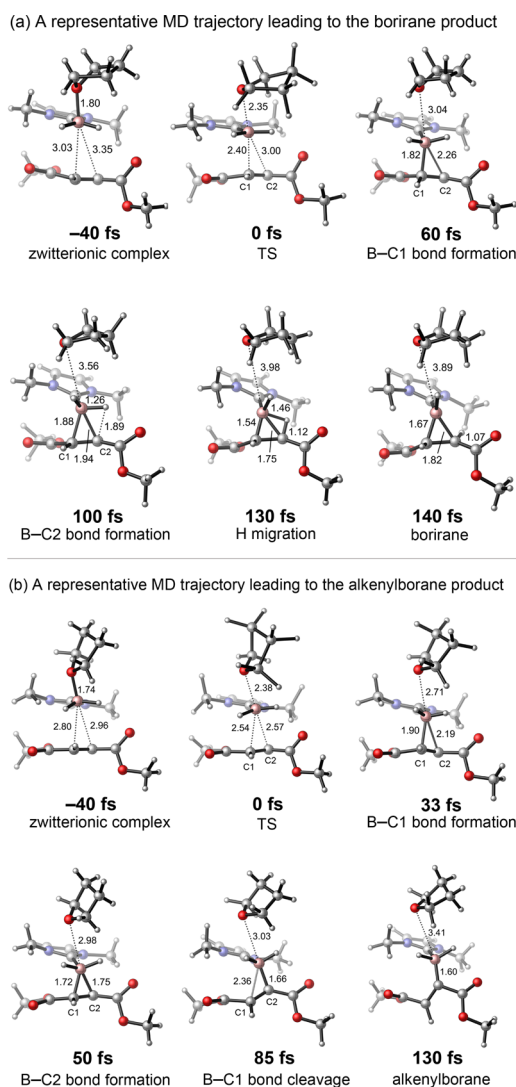


Figure 6. Snapshots of molecular dynamics trajectory simulations of the reaction of **5a** and **6**. Notice that the (a)/(b) pair of trajectories look grossly similar in the first set of three frames before diverging in the second set of three frames.

The formation of a borirane **7** from an NHC-borane **5** and acetylenedicarboxylate **6** is, formally, a double hydroboration reaction. Thus, four bonds are broken (two B–H bonds of **5** and both π -bonds of **6**) and four bonds are formed (two borirane B–C bonds and two borirane C–H bonds).

A sensible stepwise mechanism for this double hydroboration is by way of the single hydroboration product (Figure 4).¹⁰ Alkenylborane **8** could undergo a 1,2-hydride shift to give a zwitterionic species like **9**, a borenium ion/ester enolate that would quickly collapse to **7**. This would mean either that **8** is the immediate precursor of **7** or that **7** and **8** are in equilibrium. Both possibilities were ruled out by control experiments and calculations (see SI).¹⁵ Briefly, pure samples of products **7a–d** and **8a–d** are stable, and do not interconvert on storage at rt or heating in solution. The thermal stability of the boriranes is striking. For example, the ^1H NMR spectrum of **7d** is essentially unchanged after heating for 1 week at 80°C in acetonitrile.

With the understanding that borirane **7** and alkenylborane **8** are both primary reaction products, we performed density functional theory (DFT) calculations to investigate pathways for their formation. The DFT calculations were performed at the M06-2X/6-311++G(d,p)//M06-2X/6-31G(d) level of theory and the SMD solvation model in THF. The most favorable pathways in the reaction of NHC borane **5a** and **6** are shown in Figure 5.

The initial hydride transfer from NHC-borane **5** to **6** is highly *trans*-selective to form a weakly bound zwitterionic complex of the NHC borenium and the alkenyl anion **10**. The corresponding *cis*-selective hydride transfer (SI) requires 5.0 kcal/mol higher activation free energy. Upon coordination with a THF solvent molecule, the borenium is converted to a more stable four-coordinated boronium cation, which forms an ion pair with the alkenyl anion **11**. Subsequent addition of the THF-coordinated borenium to the alkenyl anion occurs via **TS2-THF**, in which the boronium approaches the π orbital that is perpendicular to the plane of the alkenyl anion. Although this geometry resembles the classical four-membered alkene hydroboration transition state,¹⁶ the B–H bond in **TS2-THF** is short (1.19 Å), suggesting this TS may not directly lead to B–H bond cleavage.

To identify the product formed from the borenium addition transition state **TS2-THF**, we performed quasi-classical Born–Oppenheimer molecular dynamics (BOMD) trajectory simulations.^{16a,17} The initial geometries and velocities for the BOMD trajectories were generated from the normal mode sampling of **TS2-THF** at 298 K. The trajectories were propagated using the classical equations of motion with energies and forces computed using M06-2X/6-31G(d) in THF with the SMD solvation model.

Out of the 100 trajectories calculated, the alkenylborane product **8a** is formed in 85, and the borirane product **7a** is formed in 15. These results are roughly consistent with

experiment (Table 1, entry a) and indicate that a single transition state TS2·THF leads to both the alkenylborane and the borirane products via a bifurcating reaction pathway in which no stable intermediates or transition states exist between the TS and the two final products.¹⁸

Snapshots of two representative BOMD trajectories that lead to the borirane and the alkenylborane products are shown in Figure 6a and 6b, respectively. Both trajectories start by shortening of the B–C1 bond, followed by the decrease of the B–C2 bond distance. Then the two trajectories diverge. In the trajectory leading to the alkenylborane product (Figure 6b), the B–C1 bond is cleaved after 85 fs. In contrast, a 1,2-hydrogen migration occurred in the trajectory shown in Figure 6a, which leads to the formation of the C–H bond in the borirane product.

In summary, we have discovered a formal double hydroboration reaction of acetylenedicarboxylates by NHC-boranes to give stable NHC-boriranes. Eight bonds are involved: four broken and four formed. Despite that, the transformation is compact, bringing three atoms (a boron and two carbons) together into a small ring. This simple yet remarkable reaction is in competition with a 1,2-hydroboration reaction to give (*E*)-alkenylboranes. DFT calculations suggest a mechanism where divergence to the two products occurs after a common initial stage of hydride transfer from the NHC-borane to the acetylenedicarboxylate. The *N*-substituents on the NHC-borane play an important role, with large *N*-aryl substituents giving slower reactions (compared to *N*-alkyl groups) but increased amounts of borirane at the expense of alkenylborane. The ease of synthesis and stability of these rare boriranes open the door to study of their chemistry and properties.

■ ASSOCIATED CONTENT

■ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b09873.

Details of experiments and calculations (PDF)

Data for C₁₅H₂₅BN₂O₄ (CIF)

Data for C₂₇H₃₃BN₂O₄ (CIF)

Data for C₃₃H₄₅BN₂O₄ (CIF)

Data for C₂₇H₃₃BN₂O₄ (CIF)

Data for C₃₃H₄₅BN₂O₄ (CIF)

Movie of trajectory (MPG)

Movie of trajectory (MPG)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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