Selective boryl-anion migration in a vinyl sp²-sp³ diborane induced by soft borane Lewis acids

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Abstract: A novel intramolecular 1,2-boryl anion migration from boron to carbon has been achieved by selective activation of the π-system in [(vinyl)B₂Pip₃] using “soft” Br₂ electrophilic (Br₂ = BPh₃ or 9-Aryl-BBN). The soft character is key to ensure 1,2-migration proceeds instead of oxygen coordination / B-O activation. The Br₂ induced-1,2-boryl anion migration represents a triple borylation of a vinyl Grignard reagent using only B₂Pip₃ and Br₂ and forms differentially protected 1,1,2-triborylated alkanes. Notably, by increasing the steric bulk on the beta position of the vinyl Grignard reagent used to activate B₂Pip₃, 1,2-boryl-anion migration can be suppressed in favor of intermolecular {BPin} transfer to BPh₃, which represents a simple way to access unsymmetrical sp³-sp³ diboranes.

The coordination of Lewis bases (LB) to diborane(4) compounds, such as B₂Pip₂ (1), generates an sp³-sp³ diborane in which the boron–boron bond is polarized. ¹ This imparts nucleophilic character to the sp³ boron, thereby enabling the mild generation of a functional equivalent of (BPin)⁻.² This has become a powerful transition metal free methodology to borylate organic substrates and generate desirable organoborane esters. Alkoxides or N-heterocyclic carbenes (NHCs) are the typical LBs employed in the activation of ¹,³ with the use of carbanions (R⁻) having much less precedence,⁴⁻⁹ despite R⁻ being able to generate a more nucleophilic (BPin)⁻ moiety due to their greater basicity relative to alkoxides and NHCs. Among the limited examples in this area, recent work has shown that complex A synthesised from 1 and nBu-MgL (L = β-diketiminato) transfers a boryl anion to form borylated unsymmetrical sp³-sp³ diboranes (Scheme 1, 1a).⁻¹² Indeed, transfer of a boryl nucleophile to an external electrophile is the dominant reactivity pathway reported for B₂Pip₂ activated by simple diboranes. ¹³ It is important to extend the chemistry of [(R)B₂Pip₃] to allow new routes to highly functionalized organoboranes to be discovered, as these will be desirable particularly if accessed using readily accessible starting materials (e.g. RMgX / B₂Pip₂).

Prior to this work, 1,2-boryl-anion migration from boron to carbon in [(R)B₂Pip₃] species had been limited to using functionalized “R⁻” equivalents. For example, coordination of a carbanion containing a Br or OCB group (or a diazokane), to 1 led to loss of [OCb]⁻, [Br⁻] (or N₂) and formation of 1,1-diborylalkanes (Scheme 1, 1b).⁻¹¹⁻¹² We hypothesised that an alternative route to induce intramolecular 1,2-boryl-anion migration would be the activation of an unsaturated R group (e.g. -CH=CH₂) in [(R)B₂Pip₃] by a borane Lewis acid. This is attractive as it avoids prefunctionalization of the carbanion activator. This approach is conceptually related to the Zweifel reaction,¹⁵ but the use of borane Lewis acids and [BPin]⁻ as the migrating group will lead to differentially functionalised 1,1,2-triborylated alkanes in one step. Related 1,1-diborylated alkanes have emerged as highly versatile reagents used in selective C-C bond formation by the Suzuki-Miyaura coupling reaction or via deprotonation / deborylation of the diborylated carbon.¹⁶⁻²²

The selective (for intramolecular 1,2-boryl-migration) activation of [(vinyl)B₂Pip₂] (complex B, Scheme 1 bottom), requires judicious choice of the borane, Br₃, as a range of outcomes are feasible including: (i) vinyl anion transfer from B to Br₃; (ii) binding of Br₃ to an oxygen in B and subsequent C-O or B-O cleavage; (iii) [BPin]⁻ anion transfer from B to Br₃; (iv) Br₃ activation of the vinyl π-system and intramolecular [BPin]⁻ transfer. While (i) and (ii) are undesirable, pathway (iii) would be an attractive route to unsymmetrical diboranes using commercial Grignard reagents as activators. Equally notable and our primary focus - intramolecular 1,2-boryl-migration (pathway iv) - would be a new and simple route to 1,1,2-triborylated alkanes.

Previous work

1a) Intermolecular [BPin]⁻ transfer with a (β-diketiminato)Mg complex

1b) Intraoatomic [BPin]⁻ transfer with preinstilled leaving group

This work: Selective intraoatomic (BPin)⁻ transfer

Scheme 1. Top, previous work on intermolecular / intramolecular (BPin)⁻ transfer in carboration activated B₂Pip₂. Bottom, selective boryl-anion migration in vinyl sp²-sp³ diboranes induced by soft borane Lewis acids.

Herein, we report that intramolecular 1,2-boryl-migration in sp³-sp³ diboranes does not require preinstilled leaving groups in the carboration. Instead the formation of [(vinyl)B₂Pip₂] followed by selective activation of the π system by certain boranes forms differentially functionalised (at boron) 1,1,2-triborylated alkanes. The use of β-methyl vinyl Grignard reagent changes the reaction outcome to intermolecular (BPin)⁻ transfer to Br₃, generating an unsymmetrical diborane from simple starting materials.
We started our investigation by probing the accessibility of the simplest vinyl adduct of 1, \([\text{[CH}_2=\text{CH}]_2\text{BPin}_2]^{-}\) \([2]\). This could be generated as the major product by the addition of 1 equiv. of commercial vinyl magnesium bromide to 1 in THF at \(-78^\circ\text{C}\) (Scheme 2, left). The successful formation of \([2]\) was indicated by \(^{11}\text{B}\) NMR spectroscopy where two new resonances could be observed: one at 37.3 ppm (three coordinate boron) and the other at 4.8 ppm (four coordinate boron), analogous with that reported for \([\text{[PH}_2\text{BPin}_2]^{-}\) \((39.2\text{ and }4.0\text{ ppm, respectively).}^6\) Since \(\text{B(C}_6\text{F}_5)_3\) can activate alkenes and alkynes even in the presence of certain oxo-functionalities, the ability of \(\text{B(C}_6\text{F}_5)_3\) to trigger the 1,2-boryl-migration was explored.\(^{22}\) Adding 1 equiv. of \(\text{B(C}_6\text{F}_5)_3\) to \([2]\) \((\text{at }-78^\circ\text{C})\) led after 2 hours to a single new \(^{11}\text{B}\) resonance at -3.2 ppm, consistent with \([\text{RO-B(C}_6\text{F}_5)_3]^{-}\) species (in contrast [alkyl-B\(\text{C}_6\text{F}_5)_3\]) anions have a \(^{11}\text{B}\) resonance ca. -15 ppm). The \(^{19}\text{F}\) NMR spectrum confirmed \([\text{RO-B(C}_6\text{F}_5)_3]^{-}\) formation, with ESI-MS analysis supporting the formation of \([\text{RO-B(C}_6\text{F}_5)_3]^{-}\) species derived from ring opening of one BPin moiety in \([2]\). With two additional \(^{11}\text{B}\) resonances observed at 48.0 and 29.2 ppm, we tentatively assign the product as derived from \(\text{B(C}_6\text{F}_5)_3\) activation of pinacol bound to the four coordinate boron (Scheme 2, top). This is consistent with reports on BPin moieties in anionic borates undergoing B-O cleavage on addition of electrophiles.\(^{24}\)

The oxo-based reactivity of \(\text{B(C}_6\text{F}_5)_3\) with \([2]\) was attributed to the high electrophilicity and oxophilicity of this borane, therefore softer boron electrophiles were explored. In particular BPh\(_3\), since this borane reacts with complex A to generate \([\text{PinB-BPh}_3]^-\) with no competitive reactivity at the oxo-sites reported (Scheme 1, 1a).\(^{10}\) Adding 1 equiv. of BPh\(_3\) in THF to the in-situ generated \([2][\text{THF}]_2\text{MgBr}]^{-}\) \((\text{at }-78^\circ\text{C})\), resulted in the formation of the desired product \([3]\) formed from intramolecular \([\text{BPin}]^{-}\) transfer (Scheme 2, bottom). \([3]\) has diagnostic resonances in the \(^{11}\text{B}\) NMR spectrum (34.7 ppm for the C-BPin moieties, and -9.5 ppm for \([\text{C-BPh}_3]^{-}\)) and in the \(^1\text{H}\) NMR spectrum (broad signal at 0.55 ppm for the \(\text{CH}(\text{BPin})_2\)) with the formulation further confirmed by accurate mass spectrometry. Performing the reaction at \(-78^\circ\text{C}\) for 2 h and then room temperature for 18 h resulted in complete consumption of \([2]\), yielding \([3]\) in 71% (in-situ conversion) as the major product. Repeating the reaction on larger scale allowed for the isolation of \([3][\text{THF}]_2\text{MgBr}]^{-}\) as a white solid by solvent removal and washing with \(\text{Et}_2\text{O}\) (70% isolated yield). Single crystals of \([3][\text{THF}]_2\text{MgBr}]^{-}\) were obtained by layering pentane onto a THF solution (Figure 1). In the solid state structure the cation is chelated by the two pinacolato moieties of \([3]\) via oxygen coordination to magnesium. This results in a modest elongation of the B-O bonds involving oxygen coordinated to Mg (compare e and f Fig. 1). Other distances and angles in \([3][\text{THF}]_2\text{MgBr}]^{-}\) are within the expected values, with C-BPin bond distances shorter than the C-BPh\(_3\) distance (c, d vs. a, b). The oxo-based reactivity of B(C\(_6\)F\(_5\)) with \([2]\) to BPh\(_3\) followed by diboration of the vinyl group in \([\text{[CH}_2=\text{CH}]_2\text{BPin}_2]^{-}\) with B\(_2\text{Pin}_2\) (or base activated B\(_2\text{pin}_2\)) since this would yield a 1,2 arrangement of the BPin groups and not \(\pi\) coordination become significantly stronger on the NMR timescale due to chelation to Mg. Cation metathesis can be achieved using \([\text{Me}_6\text{N}]^+\text{Cl}^-\) to form the air-stable product \([3][\text{Me}_6\text{N}]\) in which the pinacol methyl groups now exhibit a single resonance in the \(^1\text{H}\) NMR spectrum at 298 K (in THF). It is noteworthy that the one-pot triborylation of a vinyl Grignard reagent has not been reported to the best of our knowledge.

Regarding the mechanism of formation, the arrangement of boranes in \([3]\) excludes the possibility of vinyl transfer from \([2]\) to BPh\(_3\) followed by diboration of the vinyl group \([\text{[CH}_2=\text{CH}]_2\text{BPin}_2]^{-}\) with B\(_2\text{Pin}_2\) (or base activated B\(_2\text{pin}_2\)) since this would yield a 1,2 arrangement of the BPin groups and not \(\pi\) coordination.\(^{12}\) To gain further insight into the reaction mechanism and the disparity between BPh\(_3\) and B\(_6\text{C}_6\text{F}_{5}\)\(_3\), DFT calculations were performed at the M06-2X/6-311G(d,p) level. Based on the structure of \([3][\text{THF}]_2\text{MgBr}]^{-}\), the cation \([\text{[THF]}_2\text{MgBr}]^-\) was included initially. The formation of the neutral adduct \(2'\) from \(1\) and the vinyl Grignard reagent is energetically favoured (\(\Delta G_{298K} = -9.8\text{ Kcal mol}^{-1}\)) despite the adverse entropic contribution (Scheme 3). Adduct \(2'\) showed a slightly elongated B-B bond relative to that of \(1\) \((1.73\text{ and }1.70\text{ Å, respectively), as reported for other sp^2-sp^3 diboranes.}^{1,2}\) Addition of BPh\(_3\) to \(2'\) to yield the product \([3][\text{THF}]_2\text{MgBr}]^{-}\) is energetically downhill (\(\Delta G_{298K} = -42.0\text{ Kcal mol}^{-1}\)) to gain insight into the disparate borane reactivity (B-O activation vs \(\pi\) activation), the change in energy upon \(\pi\) coordination to the oxygen of \(2'\) was probed. For BPh\(_3\) this process is energetically uphill (\(\Delta G_{298K} = 5.2\text{ Kcal mol}^{-1}\)), in agreement with the reduced electrophilicity and oxophilicity of this borane relative to B\(_6\text{C}_6\text{F}_{5}\)\(_3\). Replacing BPh\(_3\) with B\(_6\text{C}_6\text{F}_{5}\)\(_3\) (Scheme 3, bottom). O-coordination become significantly exergonic (\(\Delta G_{298K} = -8.8\text{ Kcal mol}^{-1}\)) consistent with the observation of B-O cleavage on mixing \([2]\) and B\(_6\text{C}_6\text{F}_{5}\)\(_3\). Thus, the correct tuning of the oxophilicity / electrophilicity of the borane employed is a key aspect to selectively trigger 1,2-boryl-migration. This is further emphasised by replacing B\(_6\text{C}_6\text{F}_{5}\)\(_3\) with
the harder Lewis acid BF$_3$, with O-coordination now becoming much more exergonic (ΔG$_{298K}$ = -26.4 Kcal mol$^{-1}$ relative to Z and BF$_3$). Attempts to crystallise [2][(THF)$_2$MgBr] were unsuccessful in our hands, thus due to the unknown exact nature of the magnesium species coordinated to [2] and to facilitate more detailed computational studies, additional DFT calculations were performed in absence of the counterion. It should be noted that the calculated HOMO and HOMO-1 of [2] are analogous to that of Z indicating that while Mg coordination will effect energies to some extent it does not drastically effect the electronic distribution. The HOMO of [2] has polarised σ-B character (consistent with the observed (BPin) nucleophilic character), as well as some σ C=C(vinyl) and lone pair oxygen character (Figure 2, left). The π C=C orbital instead contributes to the HOMO-1, with the vinyl system almost completely aligned with the B-B bond (B-B-C=C = 12.10°).

With an understanding of the reaction mechanism in hand, other soft boron based Lewis acids were tested. The addition of 1 equiv. of 9-Ph-BBN to [2] (at -78°C), gave the desired product [4], with diagnostic peaks observed in the $^{11}$B NMR spectrum (34.0 ppm for the -BPin moieties, and -15.3 ppm for [R(Ph)BBN]) and in the $^1$H NMR spectrum (upfield broad signal at 0.24 ppm for the CH(BPin)$_n$), with mass spectrometry confirming the formulation for the anion [4] (Scheme 5, top). [4][(THF)$_2$MgBr] was isolated in 52% yield (2 molecules of THF coordinated to [MgBr]$^+$ by $^1$H NMR spectroscopy). It is interesting to note that in this case the tetra-coordinated boron centre in [4] has restricted rotation causing desymmetrization of the bicyclo moiety. Notably, [4][(THF)$_2$MgBr] could be selectively deborylated by the addition of 1.1 equiv. of HNTf$_2$, which yielded 9-Ph-BBN and (Pin)$_2$:CHMe as the major products, indicating cleavage of the C-(Ph)BBN bond dominates. In contrast, (Pin)$_2$:CHMe was formed in low amounts from the addition of HNTf$_2$ to the [2], with formation of ethene and 1 dominating (Scheme 5, bottom).

This highlights the importance of using a soft Lewis acid to selectively trigger the 1,2-boryl-migration over other potential pathways. To further support that the reactivity difference between B(C$_6$F$_3$)$_3$ and BPin (or 9-Ph-BBN) is not due to steric factors (as B(C$_6$F$_3$)$_3$ is significantly bulkier than BPin), 9-mesityl-BBN and 9-o-tolyl-BBN were evaluated. While the former gave no reaction with [2] (presumably due to the large steric bulk around boron), the addition of o-tolyl-BBN to [2] in THF led to the intramolecular 1,2-boryl anion migration product [5] albeit

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**Scheme 3.** Free energy profile for formation of Z and O-coordination of the latter to the borane (the zero energy reference is set as Z + BR$_3$ in each case).**

**Scheme 4.** Free energy reaction profile for BPin$_3$ induced 1,2-boryl-migration.

**Figure 2.** The calculated HOMO and HOMO-1 of [2] (isovalue = 0.04). [2] and Z showed similar geometry (particularly regarding the B-B-C bond and HOMOs, thus the former geometry is provided and not that of [2]$^2$.**

**Scheme 5.** Top, reaction with 1, a vinyl Grignard reagent and 9-Ph-BBN. Bottom, synthesis of 1,1-diboryl-ethane via protodeboronation of [4] with this product formed in low yield from direct protonation of [2].
slower than when using 9-Ph-BBN. Importantly, no B-O cleavage products were observed, with the mass balance at this point being unreacted [2] and o-tolyl-BBN. Thus with bulkier, less Lewis acidic 9-aryl-BBN boranes the 1,2-boryl migration still proceeds selectively but it is slower, a fact further emphasised by adding 9-p-anisyl-BBN to [2], in which the 1,2-boryl anion migration proceeds to form [6] but significantly slower due to the reduced borane Lewis acidity (see SI).

With the aim to disfavour borane Lewis acids interacting with the vinylinic π system and thus switch selectivity from intra- to inter-molecular (BPin) transfer, we explored the effect of increasing steric hindrance at the β-vinylcarbon. In particular, using the adduct [7], which was generated in-situ by the addition of 1 equiv. of (E/Z)-1-propenylmagnesium bromide to 1 in THF at -78°C. The subsequent addition of BPin3 to [7] resulted in suppression of 1,2-boryl-migration with [8] detected only in trace amounts (Scheme 6). In this case [PinB-BPin] (40% yield) and (E/Z)-1-propenyl-BPin were observed as the major new species after 18 h at room temperature, thus confirming switching of selectivity from intra- to inter-molecular (BPin) transfer. This represents a simple route to access an unsymmetrical sp2-sp3 diborane using only commercial reagents.

![Scheme 6](image)

**Scheme 6.** Reaction of 1 with 1-propenyl-Grignard reagent and then BPin3. The cation is assigned as [THF-MgBr] throughout.

In summary, a novel intramolecular 1,2-boryl anion migration has been induced by the addition of soft boranes to vinyl sp2-sp3 diboranes. Competitive strong oxygen coordination has to be prevented, thus the softness of the borane is key in providing selective boryl transfer. With BPin3 and 9-Ph-BBN, intramolecular 1,2-boryl migration enables the one-pot synthesis of differentially protected 1,1,2-triborylated alkanes from simple starting materials. Furthermore, the ability to switch (BPin) transfer from intra- to inter-molecular by increasing the steric hindrance in the vinyl group allows access to unsymmetrical sp2-sp3 diboranes using commercial Grignard reagents and B3Pin2.

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**Conflict of interest**

The authors declare no conflict of interest.

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