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Hydroboration **Hot Paper**

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Hydroboration of Arynes with N-Heterocyclic Carbene Boranes**

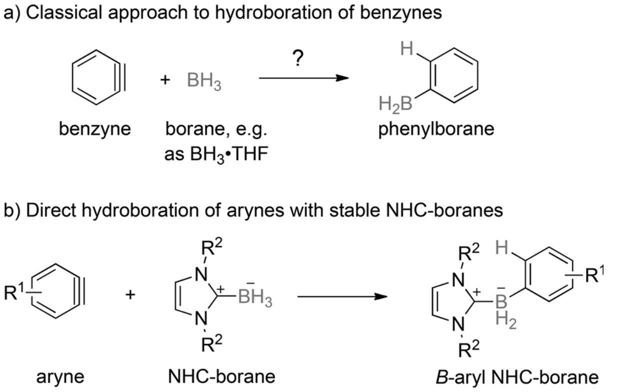
Tsuyoshi Taniguchi and Dennis P. Curran**

Abstract: *Arynes were generated in situ from ortho-silyl aryl triflates and fluoride ions in the presence of stable N-heterocyclic carbene boranes (NHC–BH_3). Spontaneous hydroboration ensued to provide stable B-aryl-substituted NHC-boranes (NHC–BH_2Ar). The reaction shows good scope in terms of both the NHC-borane and aryne components and provides direct access to mono- and disubstituted NHC-boranes. The formation of unusual ortho regioisomers in the hydroboration of arynes with an electron-withdrawing group supports a hydroboration process with hydride-transfer character.*

Hydroboration is one of the bedrock reactions of alkenes and alkynes.[1] It often occurs rapidly even in nonpolar settings. The primary hydroboration products are rarely isolated but can be converted in situ into many kinds of compounds.[2] Hydroboration reactions become increasingly rapid as π bonds become more strained.

Given this background, it might seem surprising that there are no methods for the hydroboration of benzyne and related arynes (Scheme 1 a). The hydroboration products of such highly reactive species, phenyl- or aryl-substituted boranes, have many potential uses.[2] The problem is that benzyne is generated in situ,[3] but that benzyne-forming reagents and reactive boranes are likely to be mutually incompatible. Even if a product of benzyne hydroboration manages to form, it will again be a reactive borane with the same survival problems as the starting borane.

N-Heterocyclic carbene boranes (NHC-boranes) are a class of ligated boranes with attractive features.[4] NHC complexes of the parent borane (NHC–BH_3) are easy to handle because they are stable to air, water, base, and even mild acid. They show diverse reactivity[4] that is unencumbered by the release of a reactive borane. We suspected that NHC-boranes would be stable to some of the common reagents and conditions used to make benzynes in situ.[3] At first glance, the hydroboration of benzynes does not look promising because NHC-boranes do not hydroborate alkenes and alkynes, even at high temperatures.[5] However, we felt that spontaneous hydroboration might occur, because benzynes often react as electrophiles[3] and because NHC-boranes sometimes react as weak nucleophiles (that is, hydride donors).[6] NHC-boranes are neutral, whereas the nucleophiles used in reactions of benzyne are usually anions or organometallic species. Along these lines, two attractive new boryl metalation reactions of arynes provide aryl–boron products in which the boron center has the same oxidation state as in boronic acids.[7,8]


a) Classical approach to hydroboration of benzynes

b) Direct hydroboration of arynes with stable NHC-boranes

Scheme 1. Approaches to the hydroboration of benzyne and other arynes. a) In the classical approach, the borane reagents and products may not be compatible with the reagents and conditions needed to generate benzyne. b) In the present approach, NHC-boranes are stable to aryne formation yet still spontaneously hydroborate the arynes to provide stable products.

Herein we report that benzyne can be generated in the presence of typical NHC-boranes, and that spontaneous hydroboration ensues (Scheme 1 b). The products of the hydroboration, *B*-aryl NHC-boranes, are a little-known class of molecules that have previously been prepared indirectly in three steps from boronic acids.[9] Like the parent NHC-boranes, these *B*-aryl NHC-boranes are stable compounds that are readily purified by flash chromatography.

We initially conducted three scouting experiments for the generation of benzyne in the presence of readily available 1,3-dimethylimidazol-2-ylidene borane (diMe-Imd-BH_3, **1**): 1) metal–halogen exchange of 1,2-dibromobenzene with *n*BuLi,[3] 2) thermolysis of benzenediazonium-2-carboxylate,[3] and 3) the exposure of 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**2**) to fluoride ions.[3,10] Only the third experiment provided the target product according to ^{11}B NMR spectroscopic analysis, so we focused efforts on the fluoride-mediated approach.

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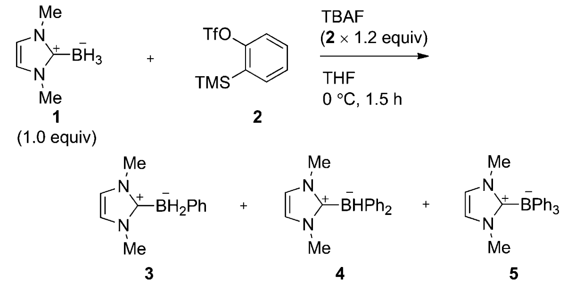
In a typical early ^{11}B NMR spectroscopic experiment, a mixture of **1** (1.0 equiv) and **2** (1.0 equiv) in THF was treated with tetra-*n*-butylammonium fluoride (TBAF, 1.2 equiv) at 0 °C. After 1.5 h, the conversion of **1** plateaued at about 50 %. We assigned the three new peaks in the spectrum to the phenyl, diphenyl, and triphenyl NHC-boranes **3**, **4**, and **5** ($\delta = -25.4$ (t), -15.9 (d), and -9.6 ppm (br s), respectively). The ratio of the products was about 83:15:2; Table 1, entry 1). The NHC-borane **1** was mostly consumed when the amount of **2** was increased to 2.0 or 3.0 equivalents, and there was a corresponding increase in the amount of diphenylborane **4** and triphenylborane **5** formed (Table 1, entries 2 and 3). Apparently, both the NHC-borane **1** and its derived products **3** and **4** are capable of the hydroboration of benzyne.

Table 1: Preliminary reactions between **1**, **2**, and TBAF.[a]



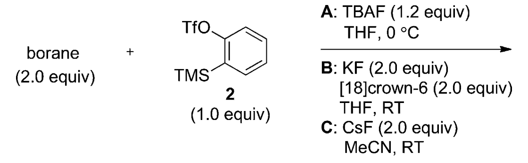
Entry	**2** [equiv]	**3**/**4**/**5**[b]	Conversion [%][b]
1	1.0	83:15:2	50
2	2.0	60:28:12	85
3	3.0	45:26:29	95

[a] Conditions: **1** (0.20 mmol), **2** (0.20–0.60 mmol), TBAF (0.24–0.72 mmol), THF (2 mL), 0 °C, 1.5 h. [b] The product ratio was estimated by ^{11}B NMR spectroscopic analysis of the crude product. Tf = trifluoromethanesulfonyl, TMS = trimethylsilyl.

On the basis of these observations, we changed the limiting reagent for preparative experiments to the benzyne precursor **2**. Reactions were conducted with NHC-borane **1** (2.0 equiv) and three different fluoride sources (Table 2, entries 1–3). The ^{11}B NMR spectrum of the crude product from the reaction with TBAF (Table 2, entry 1) showed primarily phenylborane **3** with a small resonance of diphenylborane **4** (**3**/**4** 92:8); no triphenylborane **5** was detected. Purification of this product by flash chromatography provided pure **3** (58 %) and **4** (5 %) along with a substantial amount of recovered **1** (50 %, based on starting **1**). Similar reactions conducted with potassium fluoride/[18]crown-6 (KF/18-C-6) and CsF gave comparable product ratios and yields (Table 2, entries 2 and 3). Thus, the use of 2.0 equivalents of **1** is convenient because it results in less diphenyl- and no triphenyl-substituted product, and because unreacted **1** can be readily recovered.

We next tested the reactivity of several other classes of stable borane complexes under these standard reaction conditions (Table 2, entries 4–7). Trimethylamine-borane was converted into the corresponding phenylborane $Me_3N{-}BH_2Ph$ in 32 % yield with TBAF and in 38 % yield with KF/18-C-6. No diphenyl-substituted borane ($Me_3N{-}BHPh_2$) was isolated, but no starting material was recovered either (Table 2, entries 4 and 5). In contrast, neither pyridine–borane ($C_5H_5N{-}BH_3$) nor triphenylphosphine–borane ($Ph_3P{-}BH_3$) afforded resonances for the corresponding phenylboranes in the ^{11}B NMR spectra of the crude products (Table 2, entries 6 and 7).

Table 2: Reactions of **2** with various boranes and fluoride sources.[a]



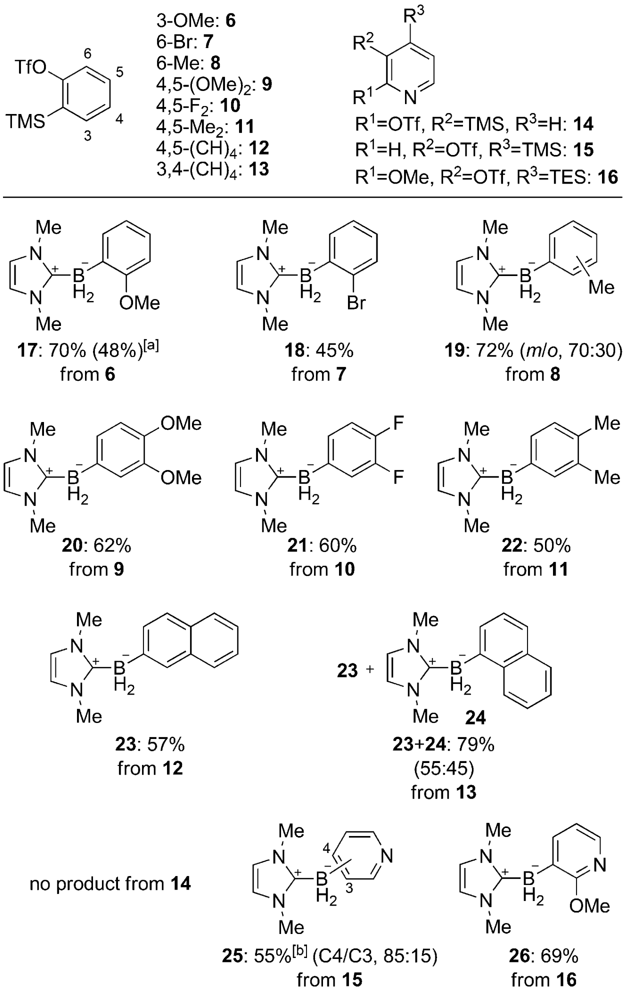
Entry	Borane	Conditions	Product (yield [%][b])
1	**1**	A	**3** (58), **4** (5), **1** (50)
2	**1**	B	**3** (61), **4** (4), **1** (60)
3	**1**	C	**3** (60), **4** (4), **1** (52)
4	$Me_3N{-}BH_3$	A	$Me_3N{-}BH_2Ph$ (32)
5	$Me_3N{-}BH_3$	B	$Me_3N{-}BH_2Ph$ (38)
6	$C_5H_5N{-}BH_3$	A	–[c]
7	$Ph_3P{-}BH_3$	A	–[c]

[a] Reaction conditions: borane (0.40 mmol), **2** (0.20 mmol), TBAF (0.24 mmol) or KF (0.40 mmol)/[18]crown-6 (0.40 mmol) or CsF (0.40 mmol), THF or MeCN (2 mL), 0 °C or room temperature, 1.5–20 h. [b] Yield of the isolated product. [c] Starting material **2** was consumed, but no target product was detected by ^{1}H and ^{11}B NMR spectroscopic analysis of the crude material.

We also tested reactions of **2** with reactive boranes not shown in Table 2, including dimethylsulfide–borane ($Me_2S{-}BH_3$) and tetrahydrofuran–borane. In these experiments, the benzyne precursor **2** remained largely intact, presumably because the borane reacted directly with the fluoride source. Pinacolborane (PinBH), catecholborane (CatBH), and 9-borabicyclo[3.3.1]nonane (9-BBN) did not afford the hydroboration product for the same reason. On the basis of this brief survey, we focused on the scope of the hydroboration of arynes by NHC-boranes.

The structures and yields of products formed in reactions of **1** (2.0 equiv) with various aryne precursors **6**–**16** (1.0 equiv) are summarized in Scheme 2. In all cases, ^{11}B NMR spectroscopic analysis of the crude product showed that the ratio of the monophenylborane to the diphenylborane product exceeded 90:10. The target monophenyl products **17**–**26** were isolated by flash chromatography along with near-theoretical amounts of recovered **1** (see the Supporting Information for full details). The minor diphenylborane product was usually but not always fully separable from the major product.[11]

The treatment of **1** and 3-methoxy-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**6**) with TBAF (conditions A) gave 2-methoxyphenylborane **17** as a single regioisomer with the two aryl substituents in an *ortho* relationship in 48 % yield. A similar reaction with KF/18-C-6 (conditions B) gave **17** in higher yield (70 %), so we favored these conditions for further experiments. The reaction of 2-bromo-6-(trimethylsilyl)phenyl trifluoromethanesulfonate (**7**) also provided 2-bromophenylborane **18** as the *ortho* regioisomer



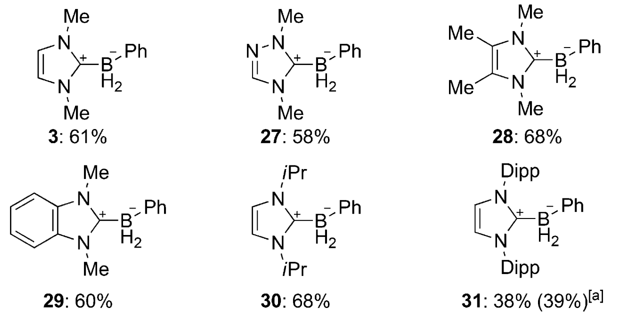
Scheme 2. Products of hydroboration reactions with NHC-borane **1**. The yields given are for the isolated product. Conditions B (Table 2) were employed unless otherwise noted. The shown numbering of **6–13** was adopted for convenience. [a] Conditions A (Table 2) were used. [b] The yield was estimated by ^{11}B NMR spectroscopic analysis of the crude material. TES = triethylsilyl.

in 45% yield, whereas that of 2-methyl-6-(trimethylsilyl)-phenyl trifluoromethanesulfonate (**8**) gave an inseparable mixture of two regioisomers of methylphenylborane **19** (*meta*/*ortho* 70:30) in 72% yield.

4,5-Disubstituted borane products **20–22** were obtained from the corresponding aryne precursors **9–11** with dimethoxy, difluoro, and dimethyl substituents in roughly comparable yield (50–62%). The precursors 1-(trimethylsilyl)-2-naphthyl trifluoromethanesulfonate (**13**) and 3-(trimethylsilyl)-2-naphthyl trifluoromethanesulfonate (**12**) were expected to give regioisomeric 1- and 2-naphthynes. The 2-naphthyne precursor **12** provided 2-naphthylborane **23** in 57% yield, whereas the 1-naphthyne precursor **13** provided an inseparable mixture of 1-naphthylborane **24** and 2-naphthylborane **23** in good yield (79%) but with low selectivity (55:45).

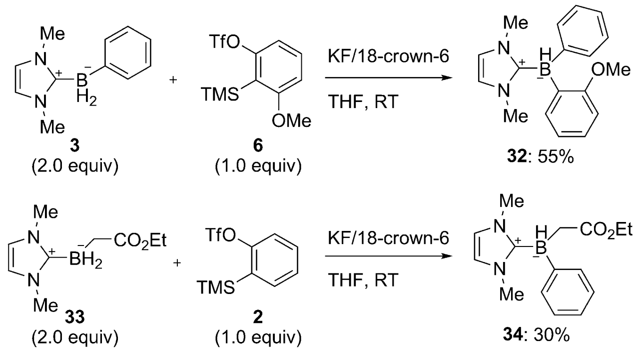
We extended this transformation to heterocycles and examined the reactions of three pyridyne[12] precursors. The precursor of 2,3-pyridyne, 3-(trimethylsilyl)pyridin-2-yl trifluoromethanesulfonate (**14**), was the only substrate that failed to provide a hydroboration product in this survey. In contrast, the 3,4-pyridyne precursors **15** and **16** reacted with **1** to provide the corresponding pyridylborane compounds **25** and **26**. The pyridylborane isomers **25** (C4/C3 85:15) were formed in about 55% yield according to ^{11}B NMR spectroscopic analysis, but were difficult to separate (see the Supporting Information). Methoxypyridine **26** was obtained as the *ortho* isomer in 69% yield. In analogy with the reaction of **6**, no *meta* isomer was observed.

Next we examined the scope of the reaction with respect to the NHC-borane component with 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**2**) as the benzyne precursor, KF/18-C-6 as the fluoride source (conditions B), and five NHCs of varying properties[13] on the borane. The structures and yields of the products are shown in Scheme 3. Reactions of dimethyltriazolylidene, tetramethylimidazolylidene, dimethylbenzimidazolylidene, and diisopropylimidazolylidene borane were similar to that of dimethylimidazolylidene borane **1** and gave the corresponding NHC-phenylborane derivatives **27–30** in 58–68% yield. In these cases, ^{11}B NMR spectroscopic analysis of the crude product showed that the ratio of the monophenylborane to the diphenylborane product exceeded 90:10 (see the Supporting Information for full details). The reaction of Dipp-protected imidazolylidene borane (Dipp is 2,6-diisopropylphenyl) with **1** and KF/18-C-6 gave **31** in 38% yield, whereas a similar reaction with TBAF provided **31** in 39% yield. With this bulky NHC-borane, the ratio of monophenylborane to diphenylborane products in the crude reaction product was excellent (ca. 96:4); however, the reaction was not as clean as in the other examples.[11]



Scheme 3. Synthesis of several NHC-phenylboranes. Conditions B (Table 2) were employed unless otherwise noted. [a] TBAF (1.2 equiv) was used instead of KF/18-C-6.

We next conducted two reactions of boron-substituted NHC-boranes to make differentially disubstituted boranes (Scheme 4). The treatment of phenylborane **3** with aryne precursor **6** and KF/18-C-6 (Scheme 4) provided unsymmetrical phenyl aryl borane **32** in 55% yield as a single *ortho* regioisomer. Furthermore, the ethyl 2-(phenylboryl)acetate NHC complex **34** was obtained from ethyl borylacetate **33** in 30% yield. In turn, **33** was prepared in one step by a rhodium-catalyzed insertion reaction between NHC-borane **1** and ethyl 2-diazoacetate (N_2CHCO_2Et).[14] Thus, the two-step synthesis of **34** from **1** involves a (formal) 1,1-hydroboration of



Scheme 4. Synthesis of two unsymmetrically disubstituted aryl boron compounds.

a carbene, followed by a 1,2-hydroboration of benzyne. These results suggest that the aryne hydroboration, either alone or coupled with other functionalization reactions of NHC-boranes, will provide unusually direct routes to diverse aryl-substituted NHC-boranes.

We consider that nucleophilic addition to benzyne may be occurring in these reactions, and that the nucleophile is a "hydride" of the NHC-borane.[6] Most nucleophilic addition reactions to benzynes bearing electron-withdrawing groups involve anions and provide *meta*-substituted products.[3] In contrast, this hydroboration reaction with neutral NHC-boranes provides *ortho*-substituted products because the hydride is the nucleophile (see Scheme 2, reactions of **6**, **7**, and **16**, and Scheme 4, first example). Tin hydrides also add spontaneously to benzyne and provide regioselectivity consistent with a hydride-addition model.[15,16] Still, it is not prudent to settle on a mechanistic model based primarily on results of preparative experiments. Radical chain mechanisms for hydroboration deserve consideration, as do more sophisticated models for addition reactions to arynes.

The ease of synthesis and stability of *B*-aryl NHC-boranes set the stage for downstream applications in both boron chemistry and organic synthesis. In the latter vein, the ready oxidation of B-unsubstituted NHC-boranes to boric acid is already known.[17] To validate this reaction with *B*-aryl NHC-boranes, we treated the B-phenyl-substituted NHC-borane **3** with dibromine (1.0 equiv) and water. As expected, phenylboronic acid ($PhB(OH)_2$) was quickly and cleanly produced. Thus, a preliminary bridge to Suzuki-type chemistry[18] is already in place.

In conclusion, we have reported the first direct hydroboration reaction of arynes. The generation of arynes by the treatment of *ortho*-silyl aryl triflates with fluoride in the presence of stable NHC-boranes led to B−aryl NHC-boranes. The stability of the NHC-borane precursors and products is crucial to the success of the hydroboration. From the standpoint of boron chemistry, the reaction shows good scope and directly provides products that were previously only available by multistep routes. From the standpoint of aryne chemistry, the unusual formation of *ortho* products from arynes bearing electron-withdrawing groups is valuable. Furthermore, recognition of the relationship between NHC-boranes and tin hydrides suggests that they may be the first members of a budding class of neutral nucleophiles that add spontaneously to arynes.

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Keywords: arynes · boranes · hydroboration · main-group chemistry · N-heterocyclic carbenes

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Communications

Hydroboration

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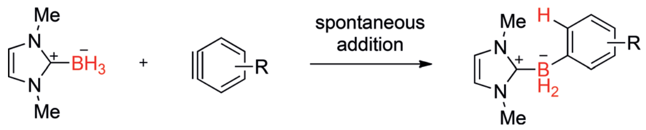
D. P. Curran* ________ ■■■■–■■■■

Hydroboration of Arynes with N-Heterocyclic Carbene Boranes



A new partnership with a future: N-Heterocyclic carbene (NHC) boranes coupled with arynes in a hydroboration reaction to produce various B-aryl-substituted NHC-boranes (see scheme), which are stable and have many potential uses. The proposed hydride-transfer character of the mechanism was supported by the *ortho* regioselectivity observed for the hydroboration of arynes with an electron-withdrawing substituent.