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Letter

Tetrahydroxydiboron-Promoted Radical Addition of Alkynols

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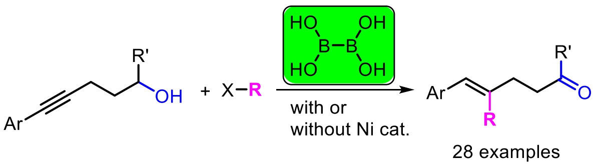
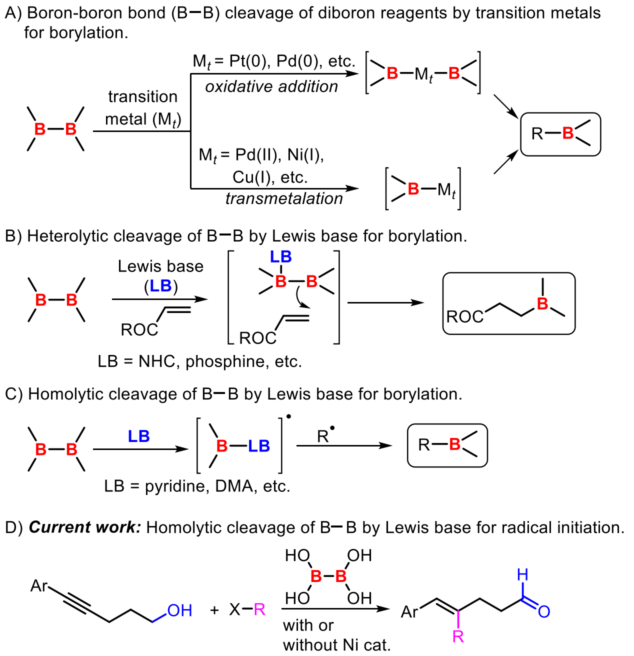
ABSTRACT: Tetrahydroxydiboron has previously been used as a borylation or reducing reagent in organic synthesis. Herein, we present a novel tetrahydroxydiboron-promoted radical addition of internal alkynes followed by intramolecular oxidation of alcohol through 1,5-hydrogen atom transfer. Preliminary mechanistic studies showed that the process might be initiated through *N*,*N*-dimethylformamide-assisted homolytic cleavage of tetrahydroxydiboron. This process provides a convenient synthesis of fluoroalkyl-substituted alkenes with a pendant aldehyde or ketone moiety.



Tetrahydroxydiboron [$B_2(OH)_4$] was first synthesized in 1950s by the hydrolysis of B_2Cl_4 and $B_2(NMe_2)_4$.[1] However, its synthetic applications in organic synthesis are far behind its derivative, bis(pinacolato)diboron (B_2pin_2), which was synthesized almost 30 years later.[2] $B_2(OH)_4$ as a borylation reagent was first explored by Szabó et al. in allylation reactions catalyzed by palladium pincer complexes.[3] Then, in 2010, Molander et al. exploited the application of $B_2(OH)_4$ for the borylation of aryl chlorides.[4] In 2017, Li et al. disclosed a decarboxylative borylation of aliphatic esters with $B_2(OH)_4$.[5] Besides serving as a borylation reagent, $B_2(OH)_4$ has also been employed as a reducing reagent to reduce pyridine *N*-oxides, azaarenes, nitroaromatics, etc.[6] To the best of our knowledge, the application of $B_2(OH)_4$ in other types of organic transformations is very limited.[7] Hydroxyl groups of $B_2(OH)_4$ might play an important role in $B_2(OH)_4$-involved reactions.[8] Herein, we will report a novel $B_2(OH)_4$-promoted reaction in which the boron radical might be formed from homolytic cleavage of the boron−boron (B−B) bond assisted by *N*,*N*-dimethylformamide.

It is well-known that diboron reagents have been widely applied in borylation reactions.[9] Transition metals have been applied in the B−B bond cleavage through two typical pathways (Scheme 1A): (1) oxidative addition of low-valent transition metals (M_t) leading to $B{-}M_t{-}B$ species,[10] a typical example being platinum-catalyzed diboration of alkynes developed by Miyaura,[10a] and (2) transmetalation with a transition metal resulting in a $M_t{-}B$ bond.[11,12] For example, Baran et al. reported a nickel-catalyzed decarboxylative borylation of alkyl *N*-hydroxyphthalimide ester by MeLi-activated B_2pin_2.[12] The resulting $M_t{-}B$ species can lead to borylated compounds by addition to unsaturated carbon−carbon bonds or cross-coupling with organic halides.

Scheme 1. Transformations Involving Diboron Reagents



Transition metal-free cleavage of the B−B bond has been widely studied recently.[13] For example, the groups of Hoveyda and Fernández independently disclosed the coordination of N-heterocyclic carbenes or phosphine with diboron leading to a polarized B−B bond to afford a nucleophilic boryl moiety (Scheme 1B).[14] In 2016, the group of Li reported the homolytic cleavage of the B−B bond by the coordination of 4-cyanopyridine.[15] Other Lewis basic reagents, such as pyridine, DMF, and DMA,[16−18] have also been involved as activators

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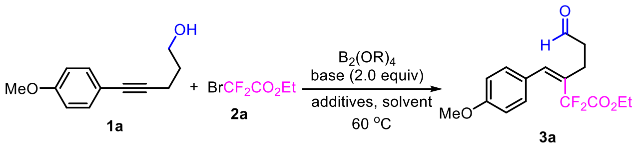
Table 1. Screening of Reaction Conditions[a]



entry	diboron reagent	solvent	base	additive	yield (%)[b]
1	$B_2(OH)_4$	DMF	K_2CO_3	–	47
2	B_2pin_2	DMF	K_2CO_3	–	4
3	B_2cat_2	DMF	K_2CO_3	–	14
4	$B_2(OH)_4$	DMA	K_2CO_3	–	41
5	$B_2(OH)_4$	DMSO	K_2CO_3	–	38
6	$B_2(OH)_4$	DCE	K_2CO_3	–	nr
7	$B_2(OH)_4$	CH_3CN	K_2CO_3	–	nr
8	$B_2(OH)_4$	THF	K_2CO_3	–	nr
9	$B_2(OH)_4$	dioxane	K_2CO_3	–	nr
10	$B_2(OH)_4$	DMF	Na_2CO_3	–	23
11	$B_2(OH)_4$	DMF	K_3PO_4	–	12
12	$B_2(OH)_4$	DMF	Cs_2CO_3	–	nr
13	$B_2(OH)_4$	DMF	DBU	–	nr
14[c]	$B_2(OH)_4$	DMF	K_2CO_3	–	20
15[d]	$B_2(OH)_4$	DMF	K_2CO_3	–	76
16[e]	$B_2(OH)_4$	DMF	K_2CO_3	$NiCl_2$·DME	75
17[e]	$B_2(OH)_4$	DMF	K_2CO_3	$NiCl_2$·DME/1,10-phen	93
18[f]	$B_2(OH)_4$	DMF	K_2CO_3	$NiCl_2$·DME/1,10-phen	92 (85)
19	–	DMF	K_2CO_3	$NiCl_2$·DME/1,10-phen	0
20	$B_2(OH)_4$	DMF	K_2CO_3	1,10-phen	42

[a] Unless otherwise noted, all reactions were performed with **1a** (0.20 mmol), **2a** (0.3 mmol, 1.5 equiv), a diboron reagent (0.10 mmol, 0.5 equiv), and a base (0.40 mmol, 2.0 equiv) in a solvent (1.0 mL) at 60 °C under Ar for 12 h. [b] Yields were determined by GC with mesitylene as an internal standard. The value in parentheses is the isolated yield. nr indicates no reaction. [c] $B_2(OH)_4$ (0.30 equiv). [d] $B_2(OH)_4$ (1.0 equiv). [e] $NiCl_2$·DME (0.10 equiv). [f] Reactions were performed on a 1.0 mmol scale in the presence of $B_2(OH)_4$ (0.20 equiv), $NiCl_2$·DME (0.01 equiv), and 1,10-phen (0.01 equiv) at room temperature.

through coordination with a boron atom, thus weakening the B−B bond. The weakened B−B bond can undergo homolysis to form the boron radical, which can further react with aryl, alkyl halides, or alkenes to form a carbon−boron bond (Scheme 1C). For example, the group of Jiao recently developed a pyridine-catalyzed radical borylation of aryl halides.[16] Meanwhile, the group of Aggarwal developed a light-initiated borylation of alkyl halides, which involves a possible DMA-assisted B−B bond homolysis.[17]

Fundamentally, if the diboron compounds, especially $B_2(OH)_4$, can be cleaved under mild conditions to give a boron radical species, it could potentially serve as a novel radical initiator, which is cheaper, more stable, and less toxic. Driven by our ongoing interest in difluoroalkyl radical reactions,[19] we explore the possibility of fluoroalkylation of alkynols promoted by $B_2(OH)_4$. Radical fluoroalkylations of alkenes have been reported followed by remote hydrogen atom translocation.[20] As mentioned above, in the presence of a Lewis base, B−B bonds might undergo homolytic cleavage to form boron radicals. Then the boron radical reacts with a fluoroalkyl halide to form the fluoroalkyl radical, which adds alkynes to form the alkenyl radical.[21,22] Then, an intramolecular 1,5-hydrogen transfer (HAT) results in an α-hydroxy carbon radical, which is liable to undergo single-electron oxidation[23] to afford a carbonyl moiety (Scheme 1D).

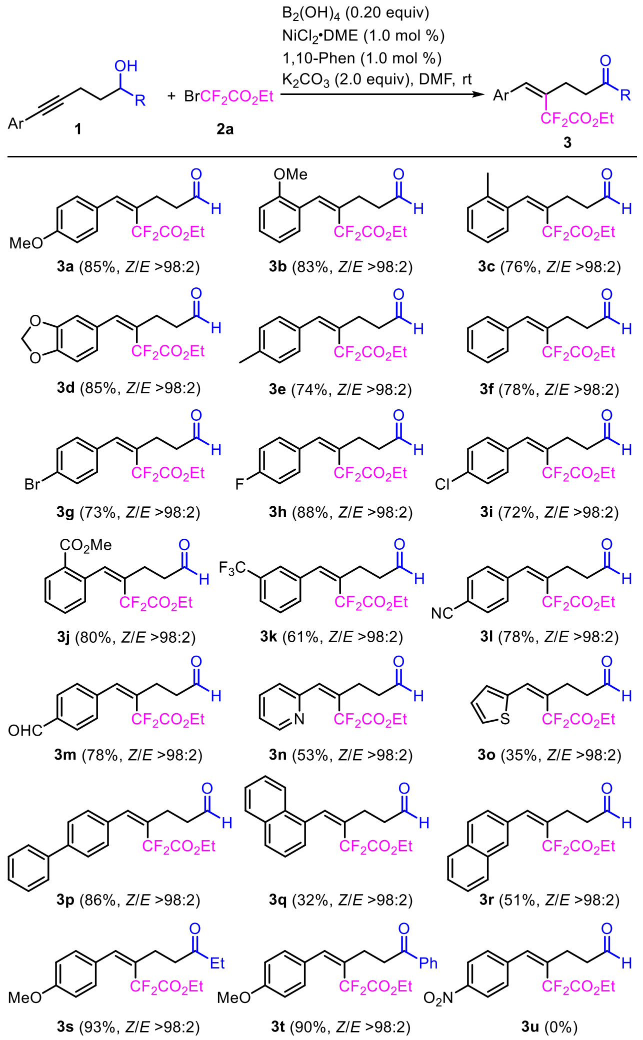
To test our hypothesis, we choose 5-(4-methoxyphenyl)-pent-4-yn-1-ol (**1a**) as a model substrate and ethyl bromodifluoroacetate (**2a**) as a fluoroalkyl radical precursor in the presence of 0.5 equiv of $B_2(OH)_4$ and K_2CO_3 in DMF at 60 °C. To our delight, the desired product **3a** was obtained in 47% yield (Table 1, entry 1). However, in the presence of B_2pin_2, only 4% **3a** was observed. When bis(catecholato)-diboron (B_2cat_2) was used, the yield of **3a** was 14% (entries 2 and 3). Therefore, the choice of the boron source is critical for the reaction to proceed smoothly, and the high reactivity of $B_2(OH)_4$ might be attributed to the presence of hydroxyl groups. Then we screened the solvents with $B_2(OH)_4$ as the diboron reagent. The yields dropped slightly in DMSO and DMA, and no expected product was observed with 1,2-dichloroethane, acetonitrile, tetrahydrofuran, and 1,4-dioxane as the solvents (entries 4−9). When K_2CO_3 was replaced with Na_2CO_3 and K_3PO_4, the yields dropped obviously to 23% and 12%, respectively. When Cs_2CO_3 and DBU were used, no expected product was detected (entries 10−13). Suspecting that the reaction might proceed through a light-induced single-electron transfer process, we conducted a control experiment in the dark and found that light has little effect on the yield (see Table S1 for details).[24]

When the amount of $B_2(OH)_4$ was decreased to 0.3 equiv, the yield dropped to 20%. On the contrary, the yield improved to 76% with 1.0 equiv of $B_2(OH)_4$ (Table 1, entries 14 and 15). Further increasing the amount of $B_2(OH)_4$ did not lead to better yields. These results indicate that $B_2(OH)_4$ was consumed during the process of reaction. Other additives were screened to increase the yields (see Table S2). It is noteworthy that addition of $NiCl_2$ improved the yield to 75% with 0.5 equiv of $B_2(OH)_4$ (entry 16). With 1,10-phenanthroline (0.1 equiv) as the ligand, the yield increased further to

93% (entry 17). Further optimization showed that in the presence of 1.0 mol % $NiCl_2$·DME and 1.0 mol % 1,10-phenanthroline, the amount of $B_2(OH)_4$ can be decreased to 0.2 equiv with the yield remaining as high as 92% (Table 1, entry 18). It is noteworthy that in the absence of $B_2(OH)_4$, no expected product was obtained (Table 1, entry 19). Given that 1,10-phenanthroline might interact with diboron to produce electron donors or radicals, an experiment with 1,10-phenanthroline was conducted in the absence of Ni(II). The result showed that 1,10-phenanthroline alone has a weaker effect on the yield (Table 1, entry 20). On the basis of screening results described above, we chose the reaction conditions in entry 18 as the optimal conditions.

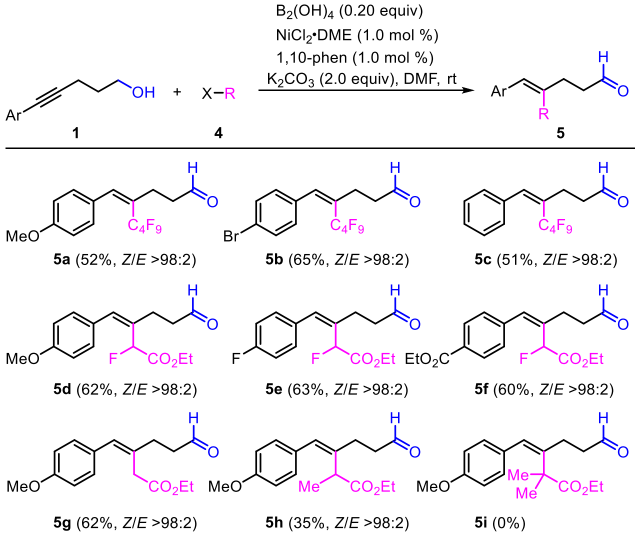
With the optimized reaction conditions in hand, the scope of alkynols was investigated (Scheme 2). Substrates containing either electron-donating or electron-withdrawing groups can be compatible under the standard conditions, resulting in target compounds **3a**−**3m** in 61−85% yields. The *Z* configuration of **3e** was determined by NOE. It is worth noting that aryl bromide in compound **3g** would readily undergo oxidative addition of Ni(0). However, no cross-coupling compound was observed, which partially indicates the absence of Ni(0) species. This protocol is also tolerant toward aza- and thia-heterocycles, although the yields were slightly lower (**3n** and **3o**). Moderate to good yields (**3p**−**3r**) were obtained with polycyclic aromatic substrates. For substrates with a secondary alcohol, the corresponding ketone products resulted in >90% yields (**3s** and **3t**). The higher yields can be ascribed to the secondary carbon-based radicals being more stable than the primary carbon-based radicals. However, the substrate containing a nitro group led to a messy mixture with no expected products (**3u**). Moreover, an alkyl acetylene substrate and aryl acetylene substrates with shorter or longer carbon chains or a functional group between the alkynyl and hydroxyl motifs have been tried, and no expected products were detected (see Scheme S1).

Scheme 2. Scope of Alkynols[a]



[a] Reaction conditions: **1** (1.0 mmol, 1.0 equiv), **2a** (1.5 mmol, 1.5 equiv), $B_2(OH)_4$ (0.2 mmol, 0.20 equiv), $NiCl_2$·DME (1.0 mol %), 1,10-phen (1.0 mol %), and DMF (5.0 mL) at room temperature for 12 h. The yields in parentheses are isolated yields. The *Z*/*E* ratio was determined by ^1H NMR analysis.

Scheme 3. Scope of Perfluoroalkyl/Fluoromethyl Halides[a]



[a] Reaction conditions: **1** (1.0 mmol, 1.0 equiv), **4** (1.5 mmol, 1.5 equiv), $B_2(OH)_4$ (0.2 mmol, 0.20 equiv), $NiCl_2$·DME (1 mol %), 1,10-phen (1 mol %), and DMF (5.0 mL) at room temperature for 12 h. The yields in parentheses are isolated yields. The *Z*/*E* ratio was determined by ^1H NMR analysis.

The scope of fluoroalkylated halides was also investigated (Scheme 3). Perfluorobutyl iodide also displayed a good reactivity and resulted in perfluoroalkylated products in moderate yields (**5a**−**5c**). Ethyl bromofluoroacetate can also be applied in this transformation in moderate to good yields (**5d**−**5f**). Remarkably, ethyl bromoacetate and ethyl 2-bromopropionate can also participate in the reaction with 62% and 35% yields, respectively (**5g** and **5h**, respectively). However, ethyl 2-bromo-2-methylpropanoate failed to produce the desired product (**5i**) perhaps due to the weak electrophilicity of the corresponding radical.

To gain insight into the role of $B_2(OH)_4$ and the nickel complex, a series of control experiments were carried out. It is possible that in the presence of Ni(II) species, the reaction proceeds through an alternative nickel-initiated radical process. However, as shown in Table 1 (entry 19), no expected product was obtained in the absence of $B_2(OH)_4$. It is possible that $B_2(OH)_4$ serves as a reducing reagent so that Ni(II) can be reduced to Ni(I), which is prone to a single-electron transfer

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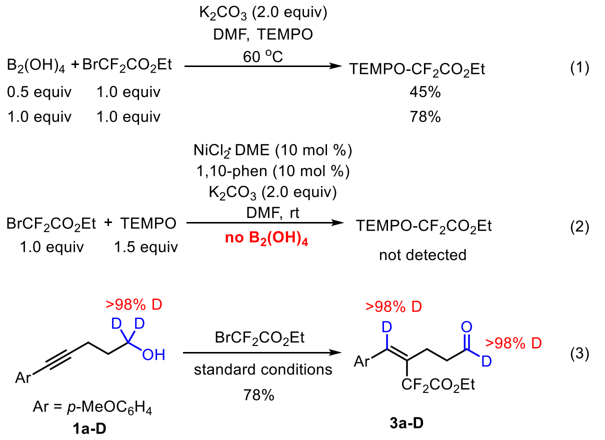
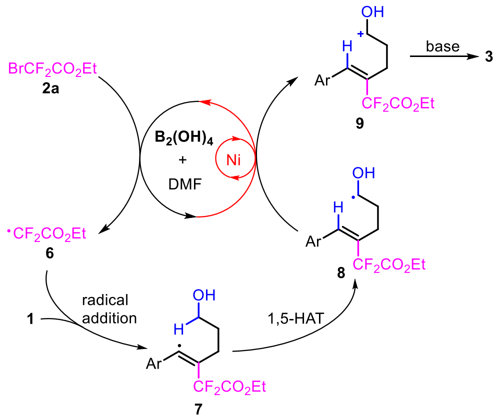
process to produce the CF_2CO_2Et radical. Therefore, Zn,[25a] Mn,[25b,c] Mg,[25d] or other stronger reductants that have been reported to be highly effective for reducing Ni(II) to Ni(I) were added to the system in place of $B_2(OH)_4$, and no product was obtained. This excludes the possibility of a nickel-initiated radical process. On the basis of these results, we proposed that $B_2(OH)_4$ might serve as the key radical initiator. To confirm this hypothesis, a typical radical scavenger, 2,2,6,6-tetramethyl-1-piperidyloxy (TEMPO), was added to the reaction mixture under standard conditions in the absence of alkyne. In the presence of 0.5 equiv of $B_2(OH)_4$, 45% TEMPO-CF_2CO_2Et was produced. When the amount of $B_2(OH)_4$ was increased to 1.0 equiv, the yield of TEMPO-CF_2CO_2Et correspondingly increased to 78% (Scheme 4, eq 1). However, when we conducted the reaction in the presence of only $NiCl_2{\cdot}DME$, no TEMPO-CF_2CO_2Et was detected, indicating that no $\bullet CF_2CO_2Et$ could be generated without $B_2(OH)_4$ (Scheme 4, eq 2). Although the detailed mechanism for formation of $\bullet CF_2CO_2Et$ promoted by $B_2(OH)_4$ is still unclear at present, the control experiments described above indicate that the formation of $\bullet CF_2CO_2Et$ is initiated by $B_2(OH)_4$. We also conducted the experiment that included deuteration to confirm the intramolecular 1,5-HAT process (Scheme 4, eq 3).

Scheme 4. Control Experiments for Mechanistic Studies



On the basis of the control experiments described above, we proposed the following mechanism as outlined in Scheme 5. First, reaction of $BrCF_2CO_2Et$ (**2a**) with $B_2(OH)_4$ in DMF affords radical $\bullet CF_2CO_2Et$ (**6**). Then $\bullet CF_2CO_2Et$ (**6**) adds to the C≡C bond of **1** to deliver a radical intermediate **7**. A 1,5-HAT process then takes place, producing radical **8**. The single-electron transfer of **8** will lead to **9**, deprotonation of which will afford **3**. In the presence of nickel, the amount of $B_2(OH)_4$ can be decreased to 0.2 equiv. The role of nickel remains unclear here, and we think it might serve as a single-electron transfer reagent.

Scheme 5. Proposed Mechanism



In conclusion, we have developed a novel tetrahydroxydiboron-promoted radical difluoroalkylation of internal alkynes followed by the 1,5-HAT process. This process provides a convenient strategy for various fluoroalkyl-substituted alkenes with pendent aldehydes or ketones. The rich abundance of functional groups in the products makes them important organic building blocks for natural product synthesis. Preliminary mechanistic studies showed that the process might be initiated by DMF-assisted $B_2(OH)_4$ homolytic cleavage resulting in a boron radical. The current protocol will open up new possibilities for application of tetrahydroxydiboron as a mild, low-toxicity radical initiator in organic transformations. Further studies to elucidate the detailed reaction mechanism are underway in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c02367.

Experimental procedures, spectral and analytical data, and copies of ^{1}H, ^{19}F, and ^{13}C NMR spectra for new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Wartik, T.; Apple, E. F. A New Modification of Boron Monoxide. *J. Am. Chem. Soc.* **1955**, *77*, 6400−6401. (b) Wartik, T.; Apple, E. F. The Reactions of Diboron Tetrachloride with Some Hydrogen Compounds of Non-Metallic Elements and with Dimethyl Sulfide. *J. Am. Chem. Soc.* **1958**, *80*, 6155−6158. (c) McCloskey, A. L.; Brotherton, R. J.; Boone, J. L. The Preparation of Boron Monoxide and its Conversion to Diboron Tetrachloride. *J. Am. Chem. Soc.* **1961**, *83*, 4750−4754.

(2) Nöth, H. Contributions to the Chemistry of Boron, 153. The Crystal and Molecular Structure of a 1,3,2-Dioxaborolan-2-yl-1',3′,2′-Dioxaborolane. *Z. Naturforsch., B: J. Chem. Sci.* **1984**, *39B*, 1463−1467.

(3) (a) Sebelius, S.; Olsson, V. J.; Szabó, K. J. Palladium Pincer Complex Catalyzed Substitution of Vinyl Cyclopropanes, Vinyl Aziridines, and Allyl Acetates with Tetrahydroxydiboron: An Efficient Route to Functionalized Allylboronic Acids and Potassium Trifluoro(allyl)borates. *J. Am. Chem. Soc.* **2005**, *127*, 10478−10479. (b) Olsson, V. J.; Sebelius, S.; Selander, N.; Szabó, K. J. Direct Boronation of Allyl Alcohols with Diboronic Acid Using Palladium Pincer-Complex Catalysis: A Remarkably Facile Allylic Displacement of the Hydroxy Group under Mild Reaction Conditions. *J. Am. Chem. Soc.* **2006**, *128*, 4588−4589.

(4) Molander, G. A.; Trice, S. L. J.; Dreher, S. D. Palladium-Catalyzed, Direct Boronic Acid Synthesis from Aryl Chlorides: A Simplified Route to Diverse Boronate Ester Derivatives. *J. Am. Chem. Soc.* **2010**, *132*, 17701−17703.

(5) Hu, D.; Wang, L.; Li, P. Decarboxylative Borylation of Aliphatic Esters under Visible-Light Photoredox Conditions. *Org. Lett.* **2017**, *19*, 2770−2773.

(6) (a) Londregan, A. T.; Piotrowski, D. W.; Xiao, J. Rapid and Selective in situ Reduction of Pyridine-N-oxides with Tetrahydroxydiboron. *Synlett* **2013**, *24*, 2695−2700. (b) Xia, Y.-T.; Sun, X.-T.; Zhang, L.; Luo, K.; Wu, L. Metal-Free Hydrogen Atom Transfer from Water: Expeditious Hydrogenation of *N*-Heterocycles Mediated by Diboronic Acid. *Chem. - Eur. J.* **2016**, *22*, 17151−17155. (c) Chen, D.; Zhou, Y.; Zhou, H.; Liu, S.; Liu, Q.; Zhang, K.; Uozumi, Y. Metal-Free Reduction of Nitro Aromatics to Amines with $B_2(OH)_4/H_2O$. *Synlett* **2018**, *29*, 1765−1768. (d) Cummings, S. P.; Le, T.-N.; Fernandez, G. E.; Quiambao, L. G.; Stokes, B. J. Tetrahydroxydiboron-Mediated Palladium-Catalyzed Transfer Hydrogenation and Deuteriation of Alkenes and Alkynes Using Water as the Stoichiometric H or D Atom Donor. *J. Am. Chem. Soc.* **2016**, *138*, 6107−6110.

(7) See some examples for the application of $B_2(OH)_4$ in other types of organic transformations: (a) Sawant, D. N.; Bagal, D. B.; Ogawa, S.; Selvam, K.; Saito, S. Diboron-Catalyzed Dehydrative Amidation of Aromatic Carboxylic Acids with Amines. *Org. Lett.* **2018**, *20*, 4397−4400. (b) Kong, W.; Wang, Q.; Zhu, J. Water as a Hydride Source in Palladium-Catalyzed Enantioselective Reductive Heck Reactions. *Angew. Chem., Int. Ed.* **2017**, *56*, 3987−3991.

(8) Baber, R. A.; Norman, N. C.; Orpen, A. G.; Rossi, J. The Solid-State Structure of Diboronic Acid, $B_2(OH)_4$. *New J. Chem.* **2003**, *27*, 773−775.

(9) (a) Xu, L.; Wang, G.; Zhang, S.; Wang, H.; Wang, L.; Liu, L.; Jiao, J.; Li, P. Recent Advances in Catalytic C-H Borylation Reactions. *Tetrahedron* **2017**, *73*, 7123−7157. (b) Yoshida, H. Borylation of Alkynes under Base/Coinage Metal Catalysis: Some Recent Developments. *ACS Catal.* **2016**, *6*, 1799−1811. (c) Kubota, K.; Iwamoto, H.; Ito, H. Formal Nucleophilic Borylation and Borylative Cyclization of Organic Halides. *Org. Biomol. Chem.* **2017**, *15*, 285−300.

(10) (a) Ishiyama, T.; Matsuda, N.; Murata, M.; Ozawa, F.; Suzuki, A.; Miyaura, N. Platinum(0)-Catalyzed Diboration of Alkynes with Tetrakis(alkoxo)diborons: An Efficient and Convenient Approach to *cis*-Bis(boryl)alkenes. *Organometallics* **1996**, *15*, 713−720. (b) Dai, C.; Stringer, G.; Marder, T. B.; Baker, R. T.; Scott, A. J.; Clegg, W.; Norman, N. C. Oxidative Addition of a B-B Bond by an Iridium(I) Complex: Molecular Structure of *mer-cis*-$[Ir(PMe_3)_3Cl(Bcat)_2]$. *Can. J. Chem.* **1996**, *74*, 2026−2031.

(11) (a) Unsworth, P. J.; Leonori, D.; Aggarwal, V. K. Stereocontrolled Synthesis of 1,5-Stereogenic Centers through Three-Carbon Homologation of Boronic Esters. *Angew. Chem., Int. Ed.* **2014**, *53*, 9846−9850. (b) Sardini, S. R.; Lambright, A. L.; Trammel, G. L.; Omer, H. M.; Liu, P.; Brown, M. K. Ni-Catalyzed Arylboration of Unactivated Alkenes: Scope and Mechanistic Studies. *J. Am. Chem. Soc.* **2019**, *141*, 9391−9400. (c) Ke, M.; Feng, Q.; Yang, K.; Song, Q. Cu-Catalyzed Hydrofluoroacetylation of Alkynes or Alkynyl Carboxylic Acids Leading Highly Stereoselectively to Fuoroacetylated Alkenes. *Org. Chem. Front.* **2016**, *3*, 150−155. (d) Fu, W.; Song, Q. Copper-Catalyzed Radical Difluoroalkylation and Redox Annulation of Nitroalkynes for the Construction of C_2-Tetrasubstituted Indolin-3-ones. *Org. Lett.* **2018**, *20*, 393−396.

(12) Li, C.; Wang, J.; Barton, L. M.; Yu, S.; Tian, M.; Peters, D. S.; Kumar, M.; Yu, A. W.; Johnson, K. A.; Chatterjee, A. K.; Yan, M.; Baran, P. S. Decarboxylative Borylation. *Science* **2017**, *356*, 1045−1053.

(13) Wen, Y.; Deng, C.; Xie, J.; Kang, X. Recent Synthesis Developments of Organoboron Compounds via Metal-Free Catalytic Borylation of Alkynes and Alkenes. *Molecules* **2019**, *24*, 101−117.

(14) (a) Lee, K.-s.; Zhugralin, A. R.; Hoveyda, A. H. Efficient C-B Bond Formation Promoted by *N*-Heterocyclic Carbenes: Synthesis of Tertiary and Quaternary B-Substituted Carbons through Metal-Free Catalytic Boron Conjugate Additions to Cyclic and Acyclic α, β-Unsaturated Carbonyls. *J. Am. Chem. Soc.* **2009**, *131*, 7253−7255. (b) Bonet, A.; Gulyás, H.; Fernández, E. Metal-Free Catalytic Boration at the β-Position of α, β-Unsaturated Compounds: A Challenging Asymmetric Induction. *Angew. Chem., Int. Ed.* **2010**, *49*, 5130−5134.

(15) (a) Wang, G.; Zhang, H.; Zhao, J.; Li, W.; Cao, J.; Zhu, C.; Li, S. Homolytic Cleavage of a B-B Bond by the Cooperative Catalysis of Two Lewis Bases: Computational Design and Experimental Verification. *Angew. Chem., Int. Ed.* **2016**, *55*, 5985−5989. (b) Wang, G.; Cao, J.; Gao, L.; Chen, W.; Huang, W.; Cheng, X.; Li, S. Metal-Free Synthesis of C-4 Substituted Pyridine Derivatives Using Pyridine-Boryl Radicals via a Radical Addition/Coupling Mechanism: A Combined Computational and Experimental Study. *J. Am. Chem. Soc.* **2017**, *139*, 3904−3910. (c) Cao, J.; Wang, G.; Gao, L.; Chen, H.; Liu, X.; Cheng, X.; Li, S. Perfluoroalkylative Pyridylation of Alkenes via 4-Cyanopyridine-Boryl Radicals. *Chem. Sci.* **2019**, *10*, 2767−2772.

(16) (a) Zhang, L.; Jiao, L. Pyridine-Catalyzed Radical Boryla- tion of Aryl Halides. *J. Am. Chem. Soc.* **2017**, *139*, 607−610. (b) Zhang, L.; Jiao, L. Super Electron Donors Derived from Diboron. *Chem. Sci.* **2018**, *9*, 2711−2722.

(17) (a) Fawcett, A.; Pradeilles, J.; Wang, Y.; Mutsuga, T.; Myers, E. L.; Aggarwal, V. K. Photoinduced Decarboxylative Borylation of Carboxylic Acids. *Science* **2017**, *357*, 283−286. (b) Wu, J.; He, L.; Noble, A.; Aggarwal, V. K. Photoinduced Deaminative Borylation of Alkylamines. *J. Am. Chem. Soc.* **2018**, *140*, 10700−10704.

(18) (a) Cheng, Y.; Mück-Lichtenfeld, C.; Studer, A. Transition Metal-Free 1,2-Carboboration of Unactivated Alkenes. *J. Am. Chem. Soc.* **2018**, *140*, 6221−6225. (b) Cheng, Y.; Mück-Lichtenfeld, C.; Studer, A. Metal-Free Radical Borylation of Alkyl and Aryl Iodides. *Angew. Chem., Int. Ed.* **2018**, *57*, 16832−16836. (c) Candish, L.; Teders, M.; Glorius, F. Transition-Metal-Free, Visible-Light-Enabled

Decarboxylative Borylation of Aryl *N*-Hydroxyphthalimide Esters. *J. Am. Chem. Soc.* **2017**, *139*, 7440−7443. (d) Sandfort, F.; Strieth-Kalthoff, F.; Klauck, F. J. R.; James, M. J.; Glorius, F. Deaminative Borylation of Aliphatic Amines Enabled by Visible Light Excitation of an Electron Donor-Acceptor Complex. *Chem. - Eur. J.* **2018**, *24*, 17210−17214. (e) Zhang, J.-J.; Duan, X.-H.; Wu, Y.; Yang, J.-C.; Guo, L.-N. Transition-Metal Free C-C Bond Cleavage/Borylation of Cycloketone Oxime Esters. *Chem. Sci.* **2019**, *10*, 161−166. (f) Chen, D.; Xu, G.; Zhou, Q.; Chung, L. W.; Tang, W. Practical and Asymmetric Reductive Coupling of Isoquinolines Templated by Chiral Diborons. *J. Am. Chem. Soc.* **2017**, *139*, 9767−9770.

(19) (a) Wang, X.; Zhao, S.; Liu, J.; Zhu, D.; Guo, M.; Tang, X.; Wang, G. Copper-Catalyzed C-H Difluoroalkylations and Perfluor-Oalkylations of Alkenes and (Hetero)arenes. *Org. Lett.* **2017**, *19*, 4187−4190. (b) Li, Y.; Liu, J.; Zhao, S.; Du, X.; Guo, M.; Zhao, W.; Tang, X.; Wang, G. Copper-Catalyzed Fluoroolefination of Silyl Enol Ethers and Ketones toward the Synthesis of β-Fluoroenones. *Org. Lett.* **2018**, *20*, 917−920. (c) Wang, X.; Liu, J.; Yu, Z.; Guo, M.; Tang, X.; Wang, G. Desulfonylation-Initiated Distal Alkenyl Migration in Copper-Catalyzed Alkenylation of Unactivated Alkenes. *Org. Lett.* **2018**, *20*, 6516−6519. (d) Yang, Y.; Yuan, F.; Ren, X.; Wang, G.; Zhao, W.; Tang, X.; Guo, M. Copper-Catalyzed Oxydifluoroalkylation of Hydroxyl-Containing. *J. Org. Chem.* **2019**, *84*, 4507−4516.

(20) (a) Yu, P.; Lin, J.-S.; Li, L.; Zheng, S.-C.; Xiong, Y.-P.; Zhao, L.-J.; Tan, B.; Liu, X.-Y. Enantioselective C-H Bond Functionalization Triggered by Radical Trifluoromethyla-tion of Unactivated Alkene. *Angew. Chem., Int. Ed.* **2014**, *53*, 11890−11894. (b) Huang, L.; Lin, J.-S.; Tan, B.; Liu, X.-Y. Alkene Trifluo-romethylation-Initiated Remote α-Azidation of Carbonyl Compounds toward Trifluoromethyl γ-Lactam and Spiro-benzofuranone-Lactam. *ACS Catal.* **2015**, *5*, 2826−2831. (c) Yu, P.; Zheng, S.-C.; Yang, N.-Y.; Tan, B.; Liu, X.-Y. Phosphine-Catalyzed Remote β-C-H Functionalization of Amines Triggered by Trifluoromethylation of Alkenes: One-Pot Synthesis of Bistrifluoromethylated Enamides and Oxazoles. *Angew. Chem., Int. Ed.* **2015**, *54*, 4041−4045. (d) Nie, X.; Cheng, C.; Zhu, G. Palladium-Catalyzed Remote Aryldifluoroalkylation of Alkenyl Aldehydes. *Angew. Chem., Int. Ed.* **2017**, *56*, 1898−1902. (e) Lonca, G. H.; Ong, D. Y.; Tran, T. M. H.; Tejo, C.; Chiba, S.; Gagosz, F. Anti-Markovnikov Hydrofunctionalization of Alkenes: Use of a Benzyl Group as a Traceless Redox-Active Hydrogen Donor. *Angew. Chem., Int. Ed.* **2017**, *56*, 11440−11444. (f) Li, L.; Ye, L.; Ni, S.-F.; Li, Z.-L.; Chen, S.; Du, Y.-M.; Li, X.-H.; Dang, L.; Liu, X.-Y. Phosphine-Catalyzed Remote α-C−H Bond Activation of Alcohols or Amines Triggered by the Radical Trifluoromethylation of Alkenes: Reaction Development and Mechanistic Insights. *Org. Chem. Front.* **2017**, *4*, 2139−2146. (g) Shu, W.; Lorente, A.; Gómez-Bengoa, E.; Nevado, C. Expeditious diastereoselective synthesis of elaborated ketones via remote Csp3−H functionalization. *Nat. Commun.* **2017**, *8*, 13832. For a review of intramolecular radical functional group migration, see: (h) Li, W.; Xu, W.; Xie, J.; Yu, S.; Zhu, C. Distal Radical Migration Strategy: An Emerging Synthetic Means. *Chem. Soc. Rev.* **2018**, *47*, 654−667.

(21) For a review of radical cascades initiated by intermolecular radical addition to alkynes, see: Wille, W. Radical Cascades Initiated by Intermolecular Radical Addition to Alkynes and Related Triple Bond Systems. *Chem. Rev.* **2013**, *113*, 813−853.

(22) (a) Benati, L.; Montevecchi, P. C.; Spagnolo, P. Free-Radical Reactions of Benzenethiol and Diphenyl Disulphide with Alkynes. Chemical Reactivity of Intermediate 2-(Phenylthio)vinyl Radicals. *J. Chem. Soc., Perkin Trans. 1* **1991**, *1*, 2103−2109. (b) Benati, L.; Capella, L.; Montevecchi, P. C.; Spagnolo, P. Free-Radical Addition of Alkanethiols to Alkynes. Rearrangements of the Intermediate.beta.-(Vinylthio) Radicals. *J. Org. Chem.* **1994**, *59*, 2818−2823. (c) Bonfand, E.; Motherwell, W. B.; Pennell, A. M. K.; Uddin, M. K.; Ujjainwalla, F. A Novel Route to 4-Aryl-5,6-dihydro-1,2-oxathiin-2,2-dioxides and Related Heterocyclic Systems. *Heterocycles* **1997**, *46*, 523−534. (d) Montevecchi, P. C.; Navacchia, M. L. Substituent Effects on Vinyl Radical Cyclizations onto Aryl Rings. *J. Org. Chem.* **1998**, *63*, 537−542. (e) Huang, L.; Ye, L.; Li, X.-H.; Li, Z.-L.; Lin, J.-S.; Liu, X.-Y. Stereoselective Radical Cyclization Cascades Triggered by Addition of Diverse Radicals to Alkynes To Construct 6(5)-6−5 Fused Rings. *Org. Lett.* **2016**, *18*, 5284−5287. (f) Wan, Y.; Shang, T.; Lu, Z.; Zhu, G. Photocatalytic 1,1-Hydrofluoroalkylation of Alkynes with a Concurrent Vicinal Acylation: An Access to Fluoroalkylated Cyclic Ketones. *Org. Lett.* **2019**, *21*, 4187−4191.

(23) De Vleeschouwer, F.; Van Speybroeck, V.; Waroquier, M.; Geerlings, P.; De Proft, F. Electrophilicity and Nucleophilicity Index for Radicals. *Org. Lett.* **2007**, *9*, 2721.

(24) An approximate estimation of pK_a(I) for tetrahydroxydiboron is 8.62 (based on SciFinder). According to the general trend of pK_a for polyprotic acid, the pK_a(II) of tetrahydroxydiboron should be around 11. Therefore, theoretically, only one hydroxyl of the tetrahydroxy diboron can be deprotonated by K_2CO_3 (the pK_a of its conjugate acid is 10.3). In addition, it is noteworthy that $B_2(OH)_4$ can be readily dissolved in DMF, but the solubility of K_2CO_3 in DMF is very poor. Therefore, the presence of K_2CO_3 should have little effect on hydrogen bonding. The major role of K_2CO_3 is to neutralize the *in situ*-generated HBr.

(25) (a) Gu, J.; Wang, X.; Xue, W.; Gong, H. Nickel-Catalyzed Reductive Coupling of Alkyl Halides with Other Electrophiles: Concept and Mechanistic Considerations. *Org. Chem. Front.* **2015**, *2*, 1411−1421. (b) Sheng, J.; Ni, H.-Q.; Zhang, H.-R.; Zhang, K.-F.; Wang, Y.-N.; Wang, X.-S. Nickel-Catalyzed Reductive Cross-Coupling of Aryl Halides with Monofluoroalkyl Halides for Late-Stage Monofluoroalkylation. *Angew. Chem., Int. Ed.* **2018**, *57*, 7634−7639. (c) Yin, H.; Sheng, J.; Zhang, K.-F.; Zhang, Z.-Q.; Bian, K.-J.; Wang, X.-S. Nickel-Catalyzed Monofluoromethylation of (Hetero)aryl Bromides via Reductive Cross-Coupling. *Chem. Commun.* **2019**, *55*, 7635−7638. (d) Cao, Z.-C.; Xie, S.-J.; Fang, H.; Shi, Z.-J. Ni-Catalyzed Cross-Coupling of Dimethyl Aryl Amines with Arylboronic Esters under Reductive Conditions. *J. Am. Chem. Soc.* **2018**, *140*, 13575−13579.