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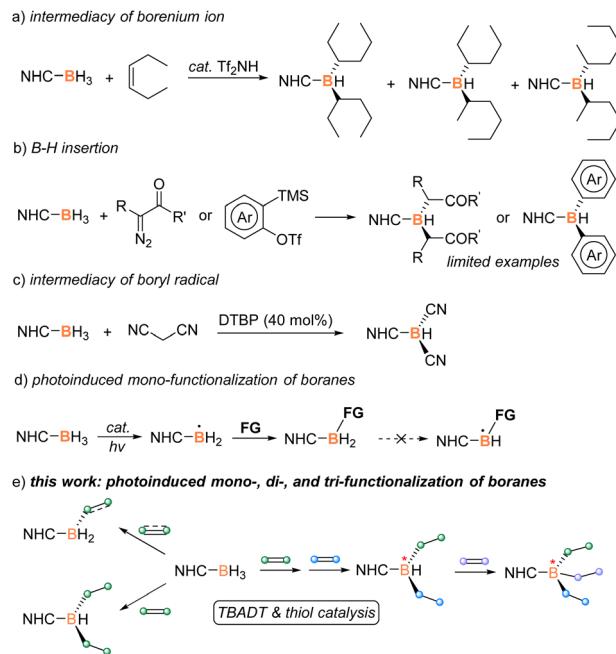
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Introduction

Organoboron chemistry has recently attracted considerable research interest due to the increasing applications of organoboron derivatives in organic synthesis, reticular materials, and pharmaceutical discovery, among others.¹ The development of powerful and selective methodologies for the preparation of new organoboron compounds is thus in urgent need.² A Lewis base borane adduct, L-BH_3 , has been proved as a readily available and moisture-stable synthon.³ Its three modifiable B–H moieties provide the possibility to be equipped with different functional groups for the design and synthesis of complex organoboron compounds. Vedejs, Curran, and Lacôte pioneered the difunctionalization of *N*-heterocyclic carbene (NHC) boranes with electron-rich alkenes *via* the intermediacy of a borenium ion (Scheme 1a).⁴ The rearrangement of the product was observed to result in a mixture of isomers. Later, Taniguchi and Curran reported stepwise B–H dialkylation and diarylation by the insertion of *in situ* generated carbenes or benzynes, however with limited examples (Scheme 1b).⁵ A boryl-radical mediated dicyanation and oxylation of NHC-borane was later developed (Scheme 1c).⁶ Recently, Pintacuda, Lacôte, and Lalevée discovered a borane–methacrylate photo-click reaction to fabricate polymers containing multifunctional NHC-boranes.⁷ Despite these seminal advances, to the best of our

knowledge, a versatile methodology enabling mono-, di-, and tri-functionalization of NHC-borane remains elusive.

Boryl-radical mediated borylation has emerged as transition-metal-free access to various organoboron compounds.⁸ The active boron-centered radical is reported to attack electron-deficient alkenes,⁹ alkynes,¹⁰ imines,¹¹ (hetero)arenes,¹² and isocyanides¹³ for the construction of new boron–carbon (B–C) bonds. However, the developed strategy has shown limited success in B–H multi-functionalization, probably because the



Scheme 1 Representative B–H functionalization of NHC Boranes.

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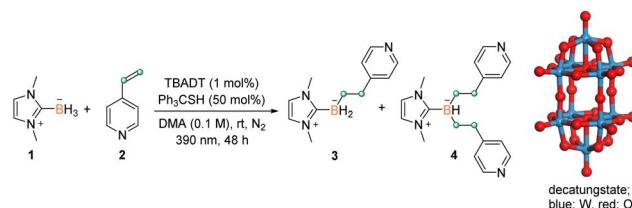
original catalytic system was not competent for the generation of boron-centered radicals from mono-functionalized boranes, the product of the first B–H activation (Scheme 1d). Therefore, a robust and versatile catalytic system is required to efficiently yield boryl radicals from mono- and di-substituted boranes for realizing their multi-functionalization. In view of the strong hydrogen-abstrating ability of excited tetrabutylammonium decatungstate (TBADT),¹⁴ we initiated a study of exploring TBADT-based catalysis for borane multi-functionalization *via* the intermediacy of boryl radicals. After many attempts, controlled mono- and di-functionalization of NHC boranes have been attained (Scheme 1e). The developed strategy also allows tri-functionalization *via* a stepwise process. The resultant multi-functionalization provides new chances for the construction of chiral boron centers and the potential development of boron atom-economic synthesis.

Results and discussion

Azaarene is arguably one of the most prevalent building blocks in bioactive and drug molecules.¹⁵ The traditional transition metal catalysis is typically inefficient for the derivatization of azaarenes due to their strong coordination to metal centers. The active open-shell radicals reportedly react with azaarenes,¹⁶ thus providing an alternative route to modifying azaarene derivatives. However, relevant investigation on boryl radicals remains relatively underdeveloped.¹² In this connection, we chose 4-vinylpyridine 2 as the model substrate, in view of the unsuccessful application of previous methods on this type of coupling partner (see Table S1† in the ESI for details).⁸ In the presence of TBADT (1 mol%) and triphenylmethanethiol (50 mol%), the treatment of NHC–borane 1 with 2 in DMA (0.1 M) under light irradiation (390 nm) at room temperature for 48 h afforded the desired disubstituted product 4 in an isolated yield of 61% (Table 1, entry 1). Using DMF or MeCN in place of DMA resulted in a mixture of mono- and di-substituted products (entries 2 and 3, Table 1). Decreasing the thiol loading to 20 mol% led to a similar inferior efficiency (entry 4, Table 1). No reaction occurred in the absence of thiol (entry 5, Table 1) and only a trace amount of 4 was detected in the absence of TBADT (entry 6, Table 1). Control experiments demonstrated that N₂ protection and light were also indispensable for this efficient disubstitution reaction (entries 7 and 8, Table 1). The complementary details for the optimization of the reaction conditions are presented in the ESI (Table S1†). Our catalyst system shows superior performance compared with previously reported ones.

With the optimized di-substitution reaction conditions (standard conditions A) in hand, we explored the substrate generality of this photoinduced di-functionalization with a series of pyridine-bearing alkenes. As shown in Scheme 2, a variety of vinylpyridines containing different substituents reacted with 1 smoothly to generate the corresponding disubstituted products 5–10 in isolated yields ranging from 50% to 62%. The use with 2-vinylpyridine gave a 34% yield of desired product 11, along with the mono-substituted product 41 (8%). Arylvinylpyridines were also compatible with the di-substitution

Table 1 Optimization of the reaction conditions^a



Entry	Variation from standard conditions	Yield [%] (3/4) ^b
1	None	0/61
2	DMF instead of DMA	27/34
3	MeCN instead of DMA	20/28
4	20 mol% of Ph ₃ CSH	18/27
5	Without Ph ₃ CSH	NR
6	Without TBADT	0/trace
7	Without N ₂	ND
8	No light irradiation	NR

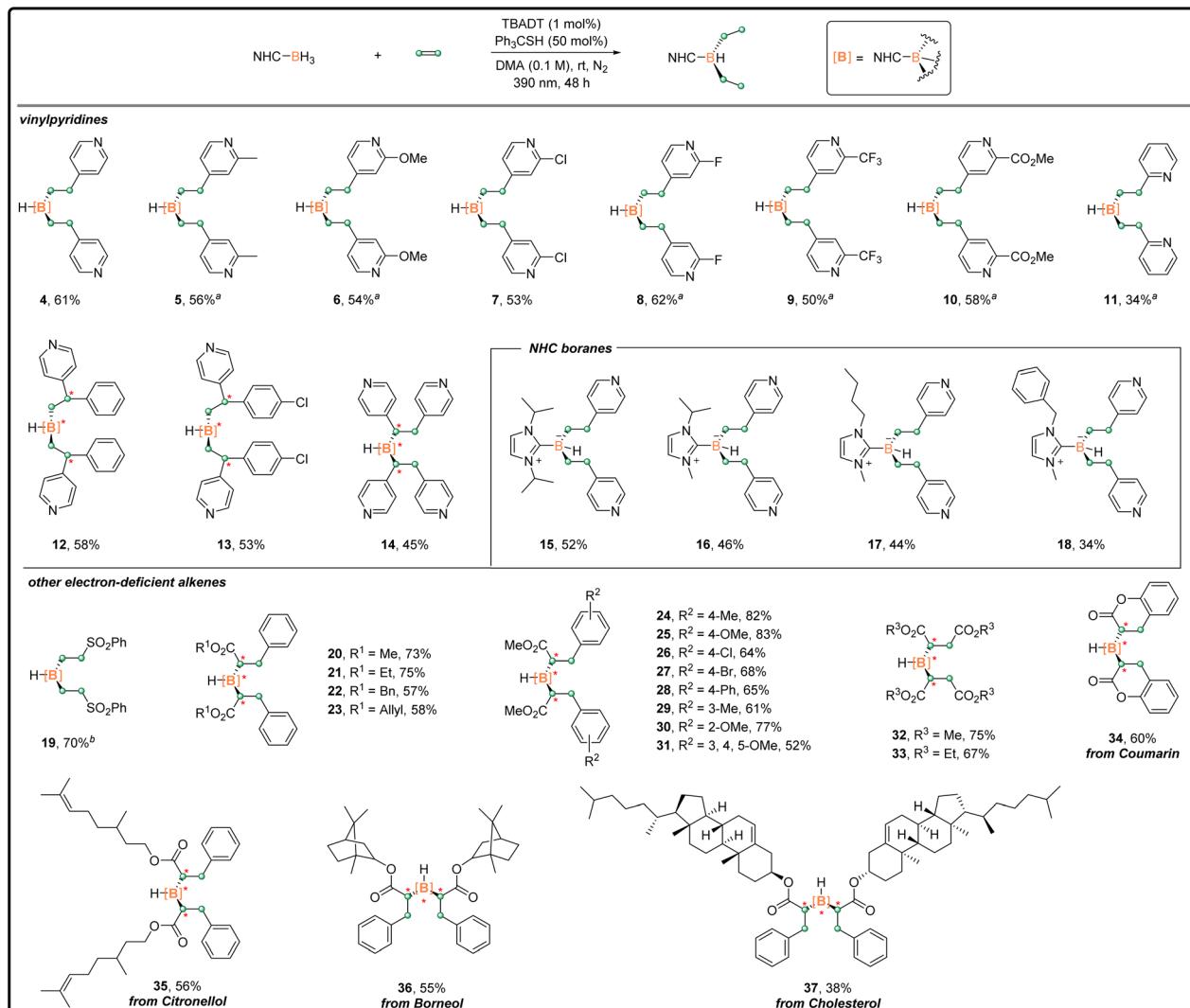
^a Standard conditions A: 1 (0.1 mmol), 2 (0.3 mmol), TBADT (1 mol%), Ph₃CSH (50 mol%), DMA (1 mL), N₂, rt, 390 nm, and 48 h; TBADT = tetrabutylammonium decatungstate. ^b The resultant mixture was first subjected to ¹¹B NMR analysis, and then flash column chromatography was carried out to give the isolated yields of the corresponding products.

reaction to deliver separable diastereomers of 12 and 13 in 58% and 53% combined yields, respectively. For these substrates, the hydroboration reaction constructed two chiral carbon centers (highlighted in red). When their stereo-configurations were different, a chiral boron center was formed. In principle, three pairs of diastereomers were produced with a ratio of 2 : 1 : 1 (see Scheme S1† in the ESI). 1,2-Di(4-pyridyl)ethylene served as a good coupling partner, giving product 14 in 45% yield. The scope of NHC–boranes was subsequently evaluated. NHC–boranes, more sterically hindered than 1, reacted with 2 well, affording the corresponding products 15–18 with moderate isolated yields.

Other electron-deficient alkenes were also examined. The utilization of phenyl vinyl sulfone provided 19 in 70% isolated yield. A wide range of cinnamate derivatives decorated with various functional groups on the ester or aryl moiety underwent the target reaction efficiently and consistently. The corresponding products were obtained in good to excellent yields (20–31, up to 83%). No obvious steric or electronic effects of the substituents were observed. It is noteworthy that the tolerated halide, ester, and olefin groups could be readily used for further functionalization. In addition, dimaleates reacted with 1 to give 32 and 33 with yields of 75% and 67%, respectively. Importantly, this methodology could be applied in the synthesis of complex organoboron compounds containing bioactive molecules or natural products, such as coumarin, citronellol, borneol and cholesterol. Moderate to good isolated yields were achieved for 34–37.

We also optimized the reaction conditions for the mono-functionalization of NHC–borane with 4-vinylpyridine (entries 13–15, Table S1† in the ESI). As shown in Scheme 3, the mono-





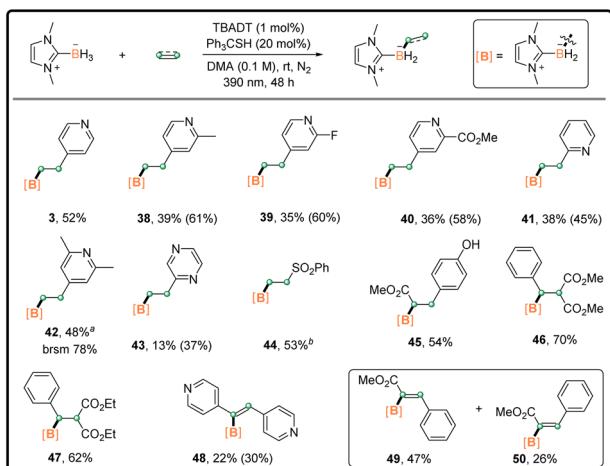
Scheme 2 Disubstitution reaction scope; general procedure A in the ESI.[†] ^a 4 equiv. of vinylpyridine was used. ^b 2.6 equiv. of phenyl vinyl sulfone was used.

substituted borane 3 was isolated in 52% yield under standard conditions B. Other vinylpyridines worked well to afford the corresponding 38–42 in moderate isolated yields. It is noted that the isolated yields for pyridine-bearing products were obviously lower than their ¹H NMR yields (~10–20% yield drop), due probably to the decomposition of products during purification. A similar yield-drop phenomenon was also observed for the purification of di-substituted boranes with pyridine substituents (Scheme 2). The substrate 2-vinylpyrazine was compatible despite the low isolated yield. Other electron-poor alkenes, including phenyl vinyl sulfone, methyl 4-coumarate, and benzylidene malonate derivatives, worked as good coupling partners. The corresponding 44–47 were obtained in 53–70% yields. Electron-deficient alkynes were also tested. Dipyridyliacetylene reacted with 1 to yield 48 with good E selectivity. In addition, the use of methyl phenylpropiolate resulted in the generation of α -borylated products 49 and 50 in 47% and 26% isolated yields, respectively. The yield is higher than that

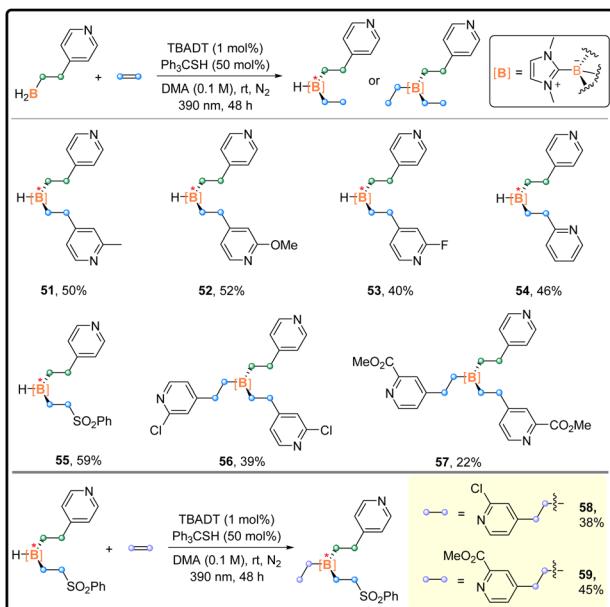
obtained by a previous method,^{10e} however with relatively moderate E/Z selectivity.

After the investigation on one-pot di-functionalization and mono-substitution, we expanded our exploration by applying the developed strategy in the synthesis of complicated organoboron compounds in a stepwise manner (Scheme 4). The installation of two different alkyl groups succeeded. The unsymmetrical products 51–55 with the stereocenter at the boron atom were attained.¹⁷ Notably, a similar stepwise method allowed the synthesis of trisubstituted boranes 56 and 57 although with relatively low isolated yields. Finally, the preparation of unsymmetrical boranes 58 and 59 bearing “quaternary boron” was realized stepwise, which can be viewed as an analogue to quaternary carbon.¹⁸ This proof-of-principle research provides new possibility for the construction of chiral boron centers.

The reactivity of representative disubstituted boranes was investigated, and the results are compiled in Scheme 5.



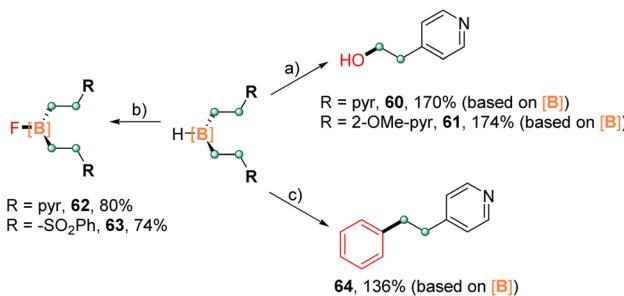
Scheme 3 Monosubstitution reaction scope; general procedure B in the ESI; [†] ¹H NMR yield in brackets; general procedure A for 42 and 44–50. ^a4 equiv. of vinylpyridine was used. ^b1.2 equiv. of phenyl vinyl sulfone was used.



Scheme 4 Diverse substitution reaction scope; general procedure C in the ESI.†

Complexes **4** and **6** underwent C–B bond oxidation with hydrogen peroxide to give the corresponding alcohols **60** and **61** in high yields (based on the boron moiety). The treatment of **4** and **19** with Selectfluor led to the fluorination products **62** and **63** in 80% and 74% yields, respectively.¹⁹ Furthermore, the Suzuki–Miyaura coupling of **4** with bromobenzene afforded the target product **64** in 136% isolated yield (based on the boron moiety). These results indicated the potential of developing boron-atom economic synthesis, that is the use of one boron atom for the functionalization of multiple carbon centers.

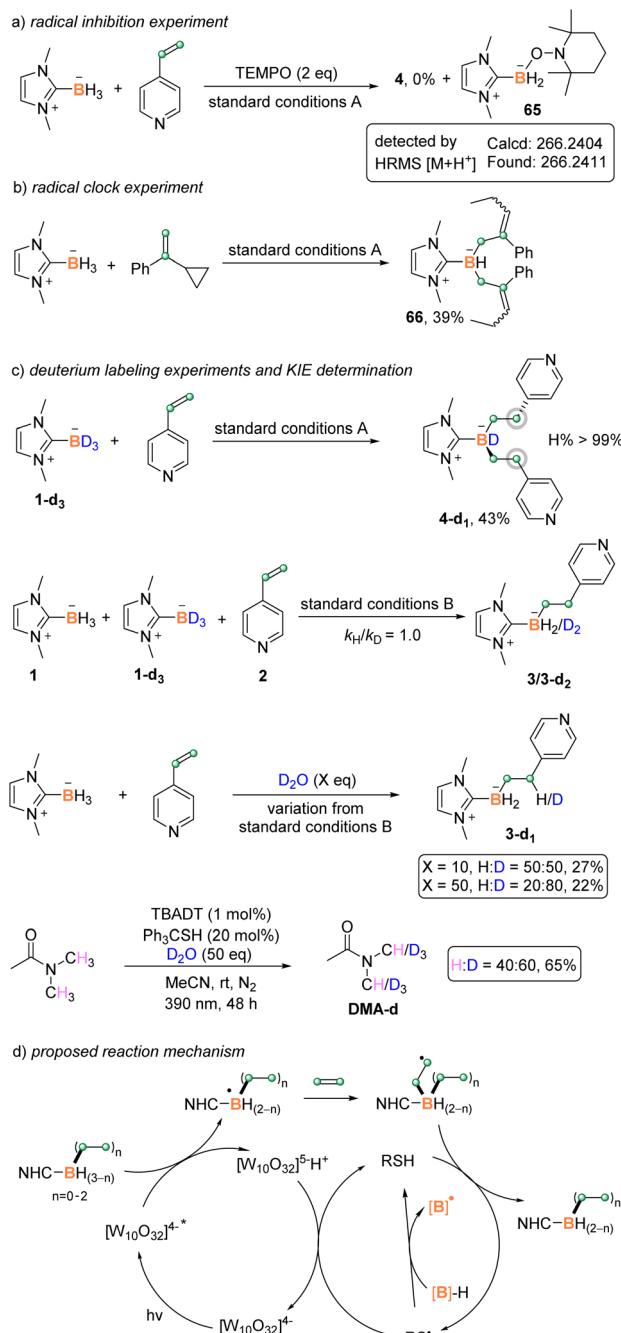
To gain more insights into the reaction mechanism, several control experiments were performed (Scheme 6). A radical



Scheme 5 Transformations. (a) H_2O_2 (8 equiv.), MeOH/MeCN, rt, and 12 h. (b) Selectfluor (1.1 equiv.), MeCN, rt, and 5 h. (c) PhBr (4 equiv.), $\text{PdCl}_2(\text{dppf})$ (10 mol%), K_3PO_4 (6 equiv.), H_2O (20 equiv.), THF, 70 °C, N_2 , and 36 h.

capture experiment was carried out by adding 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) to the reaction mixture. The disubstitution reaction was completely inhibited, and a boryl radical adduct **65** was detected by HRMS (Scheme 6a). A radical clock experiment was also conducted by using (1-cyclopropylvinyl)benzene as the substrate. Under the standard reaction conditions A, the reaction afforded the ring-opening product **66** in 39% yield (Scheme 6b). These results suggested the involvement of a boryl radical in both B–H functionalization steps. Furthermore, the kinetic isotope effect value $k_{\text{H}}/k_{\text{D}}$ of borane BH/BD was measured to be 1.0, indicating that the cleavage of B–H bond might not be involved in the rate-determining step (Scheme 6c, Fig. S7†). The replacement of **1** by NHC-BD_3 yielded the complex **4-d₁** without the deuteration of β -H of the boron atom (Scheme 6c, Fig. S4†). However, the addition of 10 or 50 equiv. of D_2O into the reaction mixture afforded the β -H deuterated product **3-d₁** with 50% and 80% deuterium incorporation, respectively (Scheme 6c, Fig. S8 and S9†). These results indicated that the β -H might originate from the hydrogen atom transfer (HAT) between the *in situ* generated β -C radical and thiol. The latter reportedly went through H/D transfer with D_2O .²⁰ Furthermore, the same catalytic system enabled the deuteration of methyl groups bonded with nitrogen in DMA (Scheme 6c), indicating the H/D exchange between DMA and thiol, which is believed to account for the little deuteration of β -H when NHC-BD_3 was used.

Based on the above experimental results and literature precedents,^{9g–i,21} a plausible reaction mechanism is proposed as outlined in Scheme 5d. Upon light irradiation, the excited TBADT abstracts a hydrogen of NHC–borane to give $[\text{W}_{10}\text{O}_{32}]^{5-}\text{H}^+$ and the NHC–boryl radical. The active boryl radical attacks the electron-deficient alkene to generate the carbon radical intermediate, which undergoes HAT with the thiol catalyst to deliver the alkylated product and a thiyl radical. Single electron transfer from $[\text{W}_{10}\text{O}_{32}]^{5-}\text{H}^+$ to the thiyl radical and the subsequent proton transfer regenerate the TBADT and thiol catalysts. Alternatively, the thiyl radical would react with borane directly to give a boron-centered radical to start another cycle. Our light on/off experiments suggested the continuation of the coupling reaction in the dark (Scheme S2† in the ESI), supporting the above HAT reaction between the thiyl radical



Scheme 6 Mechanistic studies.

and borane as well as the involvement of a radical chain pathway. A similar catalytic cycle repeats to give multi-functionalized boranes. The strong hydrogen abstraction ability of excited TBADT is believed to be important for the efficient generation of boryl radicals from substituted boranes.

Conclusions

In summary, a robust and versatile catalytic system featuring the TBADT photosensitizer has been developed for the controlled mono-, di-, and tri-functionalization of NHC-

boranes. A wide series of new organoboron compounds are obtained, which are difficult to synthesize by previous methods. The developed stepwise multi-functionalization enables the precise synthesis of unsymmetrical boranes with different substituents, providing new access to constructing chiral boron centers. The transformation of multi-substituted boranes outlines the potential of developing boron-atom economic synthesis. Pursuing the asymmetric catalytic version of multi-functionalization of boranes is underway in our lab.

Data availability

The data underlying this study are available in the ESI.†

Author contributions

Y. Q. conceived and designed the experiments. F. L., X. W., J. L., X. L., J. O., and G. H. performed experiments. F. L. and Y. Q. wrote the manuscript. Y. Q. directed the research.

Conflicts of interest

There are no conflicts to declare.

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