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## Strain-release enables access to carbonyl conjugated allylic diborons and alkenyl boronates having multiple contiguous stereocenters in a one-pot process†

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Allylic diborones are highly valuable reagents in organic synthesis. Existing methods predominantly yield alkyl-substituted allylic diborones, while the incorporation of electrophilic carbonyl groups conjugated to these allylic systems remains unknown. We present a strain-release promoted cycloaddition-based strategy that enabled access to unprecedented carbonyl conjugated secondary allylic diborones. This mild base-free method also facilitated a one-pot multicomponent cycloaddition–allylboration sequence for a highly diastereoselective installation of contiguous quaternary, tertiary and secondary carbon centers on a scaffold featuring valuable  $\beta$ -hydroxy ester,  $\beta$ -vinyl ester and vinyl boronate motifs. The synthetic utility of these densely functionalized products was demonstrated through their transformation into other rare and sterically congested alkenylborons such as borylated spiro-fused  $\beta$ -lactones and bicyclic  $\gamma$ -butyrolactones. Detailed  $^{11}\text{B}$  NMR, deuterium labeling and mass spectrometry studies provided insights on an unexpected base-free deboronative allylic shift reaction of conjugated allylic diborones.

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## Introduction

Allylic boronates represent one of the most important classes of organoborons due to their unique ability to participate in stereoselective addition reactions with aldehydes and ketones.<sup>1</sup> These allylboration reactions provide homoallylic alcohols which are ubiquitous motifs in natural products and bioactive molecules. It is, therefore, not surprising that development of novel methods to access allylic boronates and their synthetic applications has attracted significant interest.<sup>1</sup> Several creative methods have been reported for preparation of substituted allylic boronates and expand the scope of allylboration reaction. The Szabo<sup>2</sup> and Gong<sup>3</sup> groups disclosed *in situ* formation of mono allylboron via palladium catalyzed borylation followed by nucleophilic addition to carbonyl compounds. Hall and coworkers reported remarkable rate acceleration of allylboration by using Lewis acid catalysts.<sup>4</sup> They also developed mono-allyl boronates containing a 2-alkoxy carbonyl motif for activation of the boron atom.<sup>4,5</sup>

Continued progress in this area has led to the emergence of allylic geminal diborons (Scheme 1A) as allylating agents for

simultaneous installation of alkenyl boronate units on homoallylic alcohols. Murakamai<sup>6,7</sup> and Cho<sup>8,9</sup> made early contributions to the synthesis of allylic diborones (Scheme 1B). Their strategy involved Pd,<sup>6</sup> Ru<sup>7</sup> or Ir<sup>8</sup> catalyzed double bond transposition to give *E*- $\alpha$ -boryl crotyl boronates. A copper catalyzed cross-coupling of bis-boryl methyl zinc halide with vinyl iodonium salts provided  $\gamma$ -aryl/alkyl substituted allylic diboron.<sup>9</sup> Meek and coworkers developed palladium catalyzed cross-coupling of lithiated bis-boryl methane and alkenyl halides to prepare  $\gamma,\gamma$ -dialkyl allylic diborones (Scheme 1B).<sup>10–13</sup> These reagents enabled the construction of borylated homoallylic alcohols and amines having quaternary stereocenters. Chen and coworkers disclosed rhodium<sup>14</sup> and nickel<sup>15</sup> catalyzed alkene isomerization methods to afford  $\alpha$ -methyl,  $\gamma$ -methyl allylic diboron or *Z*- $\alpha$ -boryl crotyl boronates (Scheme 1B). They also developed a nickel-catalyzed 1,4-diboration approach to *Z*- $\alpha,\gamma$ -diboryl allylic borons.<sup>16</sup> Allylboration of aldehydes using these reagents provided facile stereoselective access to various *syn* and *anti* homoallylic alcohols. Recently, the Pd catalyzed Heck coupling route to allylic diborones was employed in one-pot allylboration to furnish homoallylic alcohols having adjacent secondary stereocenters (Scheme 1B).<sup>17</sup> Addition of boron to hydrazones has been used to prepare allylic monoborons and a single example of allylic diboron was reported.<sup>18</sup> An atom transfer radical annulation (ATRA) approach provided allylic diborones having a non-conjugated diester group (Scheme 1B).<sup>19</sup> Allylboration of these intermediates led to homoallylic alcohols

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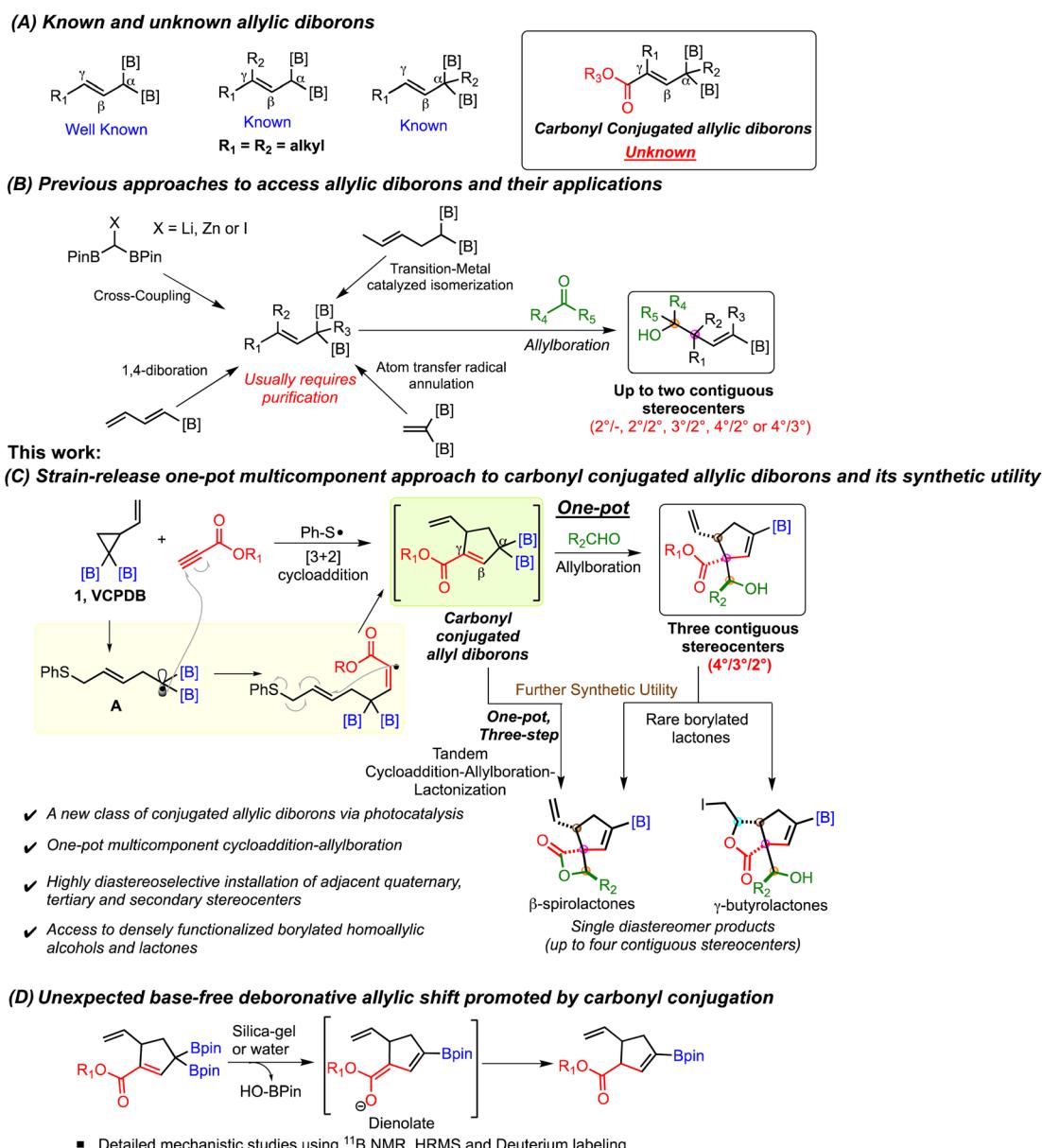


having one stereogenic center while the remote location of the ester motif from allylic alcohol precludes their intramolecular reaction.<sup>19</sup>

One of the key factors governing the versatility of the allylboration reaction is the availability of new types of substituted allylic diborons. In this context, the synthesis and allylboration of  $\gamma,\gamma$ -disubstituted<sup>10–13</sup> and  $\alpha$ -alkyl<sup>14</sup> allylic diborons (Scheme 1A) to enable stereoselective formation of quaternary carbon centers has garnered much attention. Despite the significant progress made in the synthesis of allylic diborons, there are still challenges that hinder the broader application of these geminal dimetallic reagents. The majority of the existing approaches allow synthesis of alkyl substituted allylic diborons while incorporation of electrophilic groups such as a carbonyl motif conjugated to the allylic system has remained elusive (Scheme

1A). Such conjugated systems could reveal new reactivity patterns besides opening up access to previously inaccessible highly functionalized organoborons. Furthermore, the allylboration reaction of previously known allylic diborons installs only up to two contiguous stereocenters (Scheme 1B). Finally, a metal-free one-pot strategy involving formation of functionalized  $\gamma,\gamma$ -disubstituted allyl diborons followed by their nucleophilic addition to carbonyls is unknown.

We recently developed vinyl cyclopropyl diborons (VCPDBs) as a source of homoallylic  $\alpha,\alpha$ -diboryl radicals *via* diboron-directed regioselective ring opening.<sup>20</sup> These radicals were found to undergo diastereoselective [3 + 2] cycloaddition reaction with a variety of alkenes, including acrylates. We wondered if the diboryl stabilized radicals (A, Scheme 1C) would participate in cycloaddition with propiolates under photocatalytic



Scheme 1 Strategies for synthesis and application of allylic diboranes.

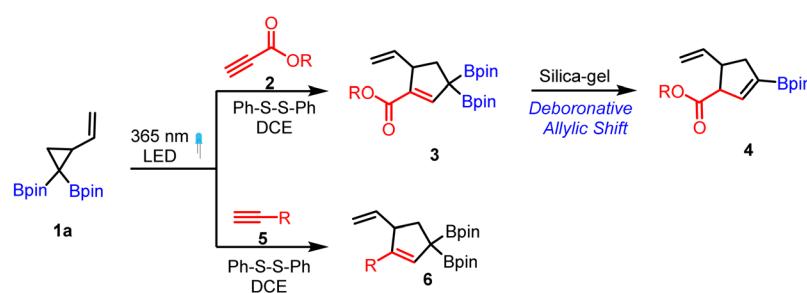


conditions. If successful, this approach would offer a direct pathway to carbonyl-conjugated allylic diborons (Scheme 1C) which would be difficult to access using conventional methods. These conjugated allyldiborons would also incorporate the desirable  $\gamma,\gamma$ -disubstituted and  $\alpha$ -alkyl motifs within the same structure. Additionally, we reasoned that the mild base-free reaction conditions enabled by thiyl radical catalysis should allow the allyldiborons to react with aldehydes in a one-pot multicomponent process. The resulting products would be densely functionalized borylated homoallylic alcohols, featuring adjacent quaternary, tertiary, and secondary carbon centers, with their relative stereochemistry defined during the allylboration step (Scheme 1C). These unique allylboration products bearing strategically located  $\beta$ -hydroxy ester and  $\beta$ -vinyl ester motifs were expected to have significant synthetic potential for construction of structurally complex organoborons *via* intramolecular reactions (Scheme 1C). Herein, we report the development of carbonyl conjugated allylic diborons as novel building blocks for direct synthesis of rare and highly

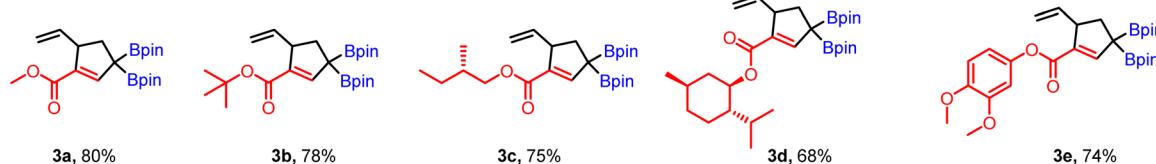
functionalized organoborons and their unexpected base-free deboronative allylic shift reaction (Scheme 1D).

## Results

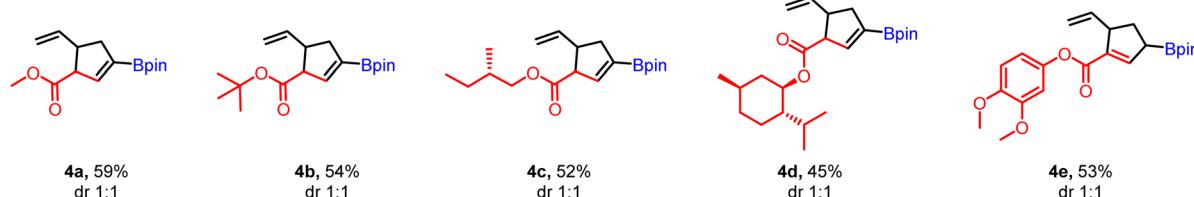
We began our studies with a reaction of VCPDB (**1a**) and methyl propiolate (**2a**) using diphenyl disulfide as a catalyst under a 365 nm LED. Surprisingly, purification of this reaction mixture *via* silica-gel chromatography provided a substituted cyclopentene (**4a**, Scheme 2) having a vinyl boronate group instead of the expected allyl boron (**3a**). <sup>1</sup>H NMR analysis of the crude reaction mixture confirmed the presence of the desired carbonyl conjugated allylic boron product (**3a**) in excellent yield (80% based on NMR, see the ESI<sup>†</sup> for details). Replacement of silica-gel with neutral alumina or use of oven-dried silica-gel for chromatographic purification also provided the deboronated product (**4a**). Further detailed investigations (see the ESI<sup>†</sup> Table 1) showed that crude **3a** is stable at room temperature under a nitrogen atmosphere up to 72 hours but it



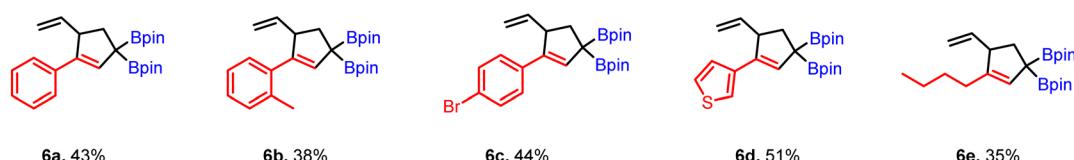
### Carbonyl conjugated allylic diborons<sup>a,b</sup>



### $\gamma$ -boryl, $\beta,\gamma$ -unsaturated esters *via* deboronative allylic shift<sup>a,c,d</sup>



### $\alpha$ -alkyl, $\gamma,\gamma$ -aryl/alkyl allylic diboronates<sup>e</sup>



**Scheme 2** Substrate scope of propiolates and alkynes for photoreaction with VCPDB. <sup>a</sup> VCPDB (**1a**, 0.31 mmol), propiolate (**2**, 0.43 mmol, 1.3 equiv.), diphenyl disulfide (0.062 mmol, 20 mol%) and DCE (1.2 mL, 0.25 M). <sup>b</sup> Yield based on <sup>1</sup>H NMR. <sup>c</sup> Reaction mixture was passed through silica gel. <sup>d</sup> both the diastereomers were isolated for **4a**–**4e**. <sup>e</sup> VCPDB (**1a**, 0.31 mmol), alkyne (**5**, 0.93 mmol, 3 equiv.), diphenyl disulfide (0.37 mmol, 1.2 equiv.) and DCE (1.2 mL, 0.25 M).



**Table 1** Optimization of the one-pot cycloaddition–allylboration reaction<sup>a</sup>

Entry	Variation from standard conditions	Yield (%)	Reaction Conditions	
			Step-1	Step-2
1	DCE as solvent in step-2	61 <sup>b</sup>		
2	None	62		
3	10 mol% diphenyl disulfide	40		
4	Toluene as solvent in step-1	51 <sup>c</sup>		
5	23 °C temperature in step-2	Trace		
6	With 4 Å MS	61		
7	10 mol% Sc(OTf) <sub>3</sub> in step-2	23 <sup>d</sup>		
8	20 mol% BF <sub>3</sub> OEt <sub>2</sub> in step-2	20		
9	5 mol% R-TRIP in step-2	28 <sup>e</sup>		
10	110 °C using Dean Stark apparatus	35 <sup>f</sup>		
11	Toluene as solvent in step-1 and benzaldehyde added in the first step (three-component reaction)	36 <sup>c</sup>		

<sup>a</sup> Standard reaction conditions: VCPDB (**1a**, 0.31 mmol), methyl propiolate (**2a**, 0.43 mmol, 1.3 equiv.), diphenyl disulfide (0.062 mmol, 20 mol%) and solvent (1.2 mL, 0.25 M), under a photoreactor for 5 h followed by removal of solvent, addition of benzaldehyde (0.62 mmol, 2 equiv.) and toluene (1.2 mL, 0.25 M) to the same pot and heating at 80 °C for 48 h. <sup>b</sup> Reaction time: 60 h. <sup>c</sup> Temp. 90 °C. <sup>d</sup> Temp. 23 °C. <sup>e</sup> Temp. 50 °C. <sup>f</sup> Reaction time: 24 h.

converts to vinylboronate (**4a**) in the presence of silica-gel, aq. acid/aq. base or even water. Such a facile deboronation under mild or neutral conditions is unusual in light of a previous report<sup>21</sup> that showed the requirement of fluoride ions or acetic acid for deborylation of allylic boronates. Interestingly, silica-gel chromatography of the reaction mixture obtained by treatment of **1a** with phenyl acetylene (**5a**) afforded the  $\gamma$ - $\gamma$ -substituted allylic boronate (**6a**, Scheme 2) instead of the vinyl boronate.

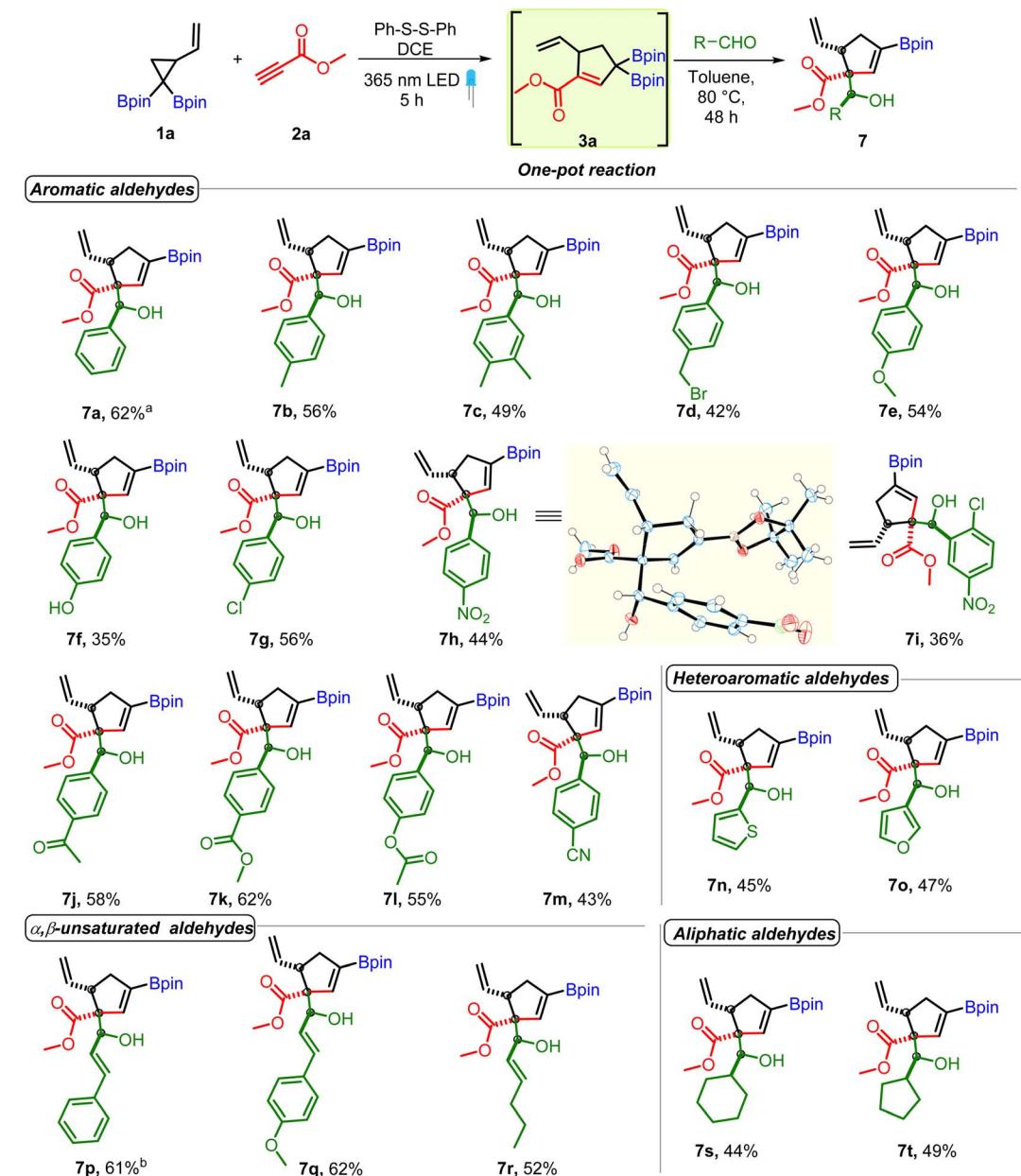
The above results suggest that the carbonyl group is the primary driver of the unusual deboronation observed in **3a**. Given the immense synthetic utility of allylic boronates and vinyl boronates, we investigated the scope of the thiyl radical catalyzed [3 + 2] cycloaddition reaction of VCPDB (**1a**) and various alkynes. A brief survey of reaction conditions showed 20 mol% phenyl disulfide catalyst in DCE as solvent to be optimal for complete consumption of the starting material. A variety of alkyl and aryl propiolates were compatible reaction partners with VCPDB (**1a**) to provide the carbonyl conjugated allylic boronates in good yield based on <sup>1</sup>H NMR analysis (**3a**–**3e**, Scheme 2). NMR analysis of the reaction mixture showed a very clean reaction with mainly the product and catalyst present at the end of the photoreaction (see the ESI†). Further scope of the propiolates including derivatives of bioactive compounds was evaluated and the results are discussed during their application for allylboration reactions (see Scheme 4). Alkynes bearing aromatic, heteroaromatic and alkyl groups were also tolerated

and the resulting allylic borons were found to be stable to silica gel chromatography (Scheme 2, **6a** to **6e**). Overall, the silica-gel induced debororative allylic shift reaction of propiolate-derived allylic boronates provided a mild strategy to access cyclic vinyl boronates containing an ester and terminal alkene functional groups. It is worth mentioning that synthesis of these cyclic  $\gamma$ -boryl,  $\beta$ - $\gamma$ -unsaturated carbonyl compounds (**4a** to **4e**) would be difficult using the hydroboration approach due to regioselectivity and chemoselectivity issues. Furthermore, the dr of these products can be increased in favor of the thermodynamically more stable *trans*-isomer by treatment of alkenyl boronates (e.g. **4a**) or allylic boron (e.g. **3a**) with a base (see the ESI† for details).

We next turned our attention to establish the synthetic utility of the photocatalytic route to conjugated allylic boronates. We wondered if the mild reaction conditions involving thiyl radical catalysis could allow for a sequential one-pot allyl boron formation and addition reaction with aldehydes. To test this hypothesis, **1a** was treated with **2a** in the presence of diphenyl disulfide as a catalyst under a 365 nm LED to form the conjugated allylic boron (**3a**). Thereafter, benzaldehyde was added to the same pot and the reaction mixture heated to 80 °C. This one-pot reaction successfully provided the desired allylboration product in very good diastereoselectivity (Table 1, entry 1). Motivated by this result, a detailed optimization of the one-pot reaction was conducted. Reducing the disulfide catalyst loading to 10 mol% or changing the solvent in the photocatalytic step to toluene lowered the yield (entries 3 and 4). Conducting the allylboration reaction at room temperature resulted in unreacted allylic boron (entry 5). However, replacing DCE with toluene as solvent before the addition of benzaldehyde reduced the reaction time while maintaining good yield (entry 2). The addition of molecular sieves or Lewis acids to promote the allylboration reaction was not beneficial (entries 6–8). Use of a chiral Brønsted acid provided the desired product (entry 9) but without inducing enantioselectivity likely because these chiral catalysts typically need low reaction temperature. Increasing the reaction temperature for the allylboration step to 110 °C and use of Dean–Stark apparatus lowered the yield (entry 10). A three-component reaction done by treating a mixture of **1a**, **2a** and benzaldehyde and disulfide catalyst in a photoreactor followed by heating to 90 °C afforded **7a** in 36% yield (entry 11). This lower yield is likely due to reduced efficiency of the photoreaction using toluene as solvent. In comparison to the allylboration reaction of previously known allylic boronates, the longer reaction time needed for reaction of **3a** with aldehyde is likely due to significant steric hindrance resulting from the presence of the  $\gamma$ , $\gamma$ -disubstituted  $\alpha$ , $\alpha$ -diboryl non-terminal allylic motif in **3a**.

The above optimized conditions were used to examine the substrate scope of the one-pot multicomponent cycloaddition–allylboration. A very broad range of aromatic and aliphatic aldehydes were found to be compatible for one-pot reaction with carbonyl conjugated allyl boron (**3a**, Scheme 3) with excellent diastereoselectivity. Benzaldehydes having electron donating groups such as alkyl, alkoxy (**7b** to **7f**) or electron withdrawing motifs like halogens or nitro at *o*, *p* or *m*-positions

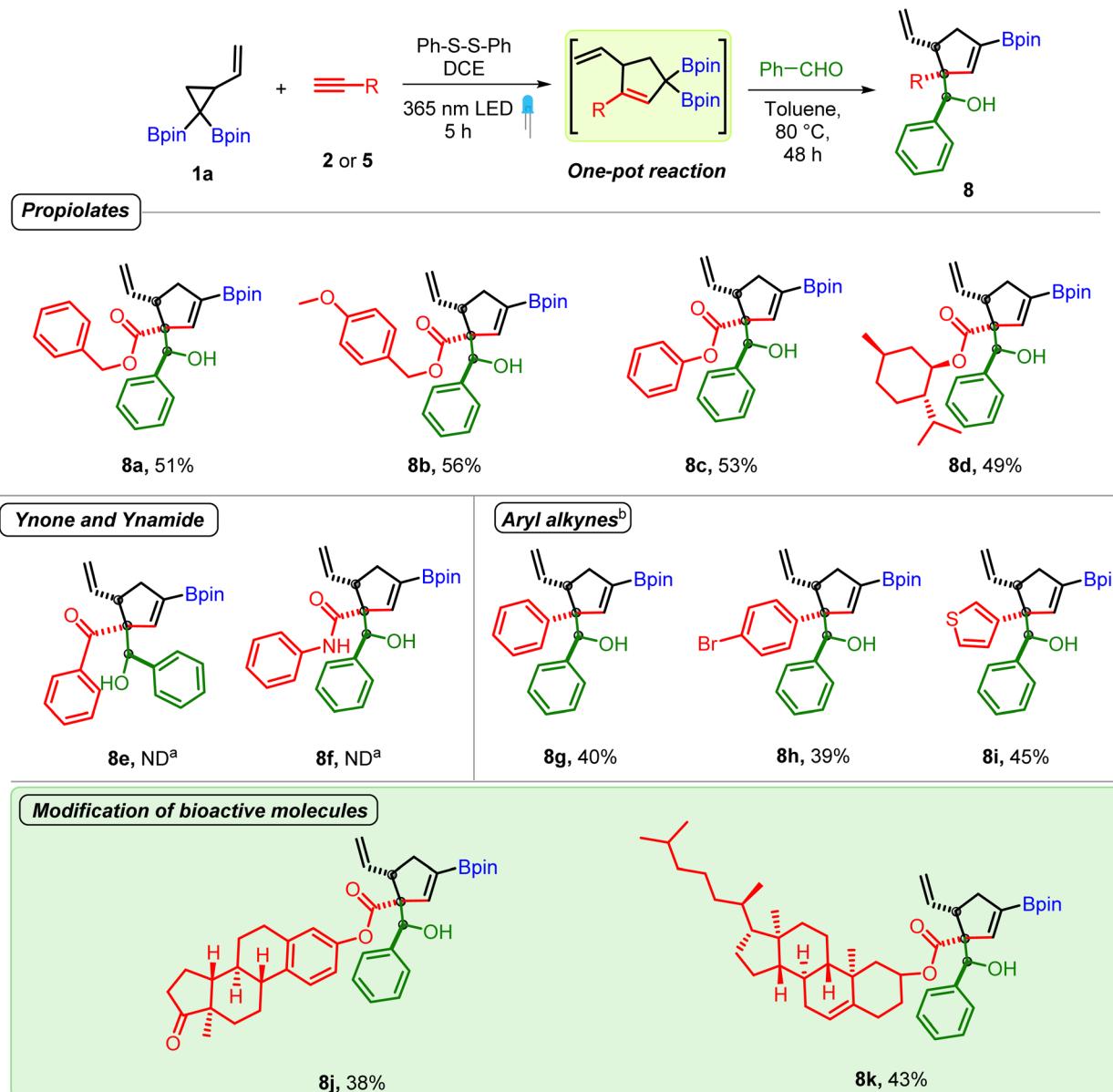




**Scheme 3** Substrate scope of aldehydes. Reaction conditions: VCPDB (**1a**, 0.31 mmol), methyl propionate (**2a**, 0.43 mmol, 1.3 equiv.), diphenyl disulfide (0.062 mmol, 20 mol%) and DCE (1.2 mL, 0.25 M), under a 365 nm LED for 5 h followed by removal of DCE and addition of aldehyde (0.62 mmol, 2 equiv.), toluene (1.2 mL, 0.25 M) to the same pot and heating at 80 °C for 48 h. <sup>a</sup> Average yield of four reactions. <sup>b</sup> Average yield of two reactions.

(**7g** to **7i**) were well tolerated. Furthermore, synthetically useful electrophilic handles such as a ketone (**7j**), ester (**7k** and **7l**) and nitrile (**7m**) could be used on benzaldehydes without compromising the yield. Heteroaromatic aldehydes (**7n** and **7o**) were compatible. The multicomponent reaction was also amenable to  $\alpha,\beta$ -unsaturated and aliphatic aldehydes (**7p**–**7t**). Other electrophiles such as ketones, imines or indoles didn't participate in the allylboration reaction with **3a** (see the ESI†). Of note, the reaction showed excellent diastereoselectivity and a single diastereomer was obtained in most cases. The relative stereochemistry was found to be *anti* on the basis of X-ray crystallography (entry **7h**, Scheme 3).

Next, we investigated the scope of alkynes. Several aryl and alkyl propiolates underwent smooth reaction thereby demonstrating the ability of highly congested carbonyl conjugated allyl borons to participate in allylboration reaction (entries **8a**–**8d**, Scheme 4). In contrast, reaction of allyl borons obtained from a ynone or ynamide didn't give the desired allylboration product (**8e** and **8f**) even as the crude reaction mixture after the photo-reaction showed the formation of corresponding carbonyl conjugated allylic boronates. On the other hand, both aromatic and heteroaromatic acetylenes proved to be competent reaction partners (**8g**–**8i**). To showcase the utility of the developed method for late-stage modification of complex



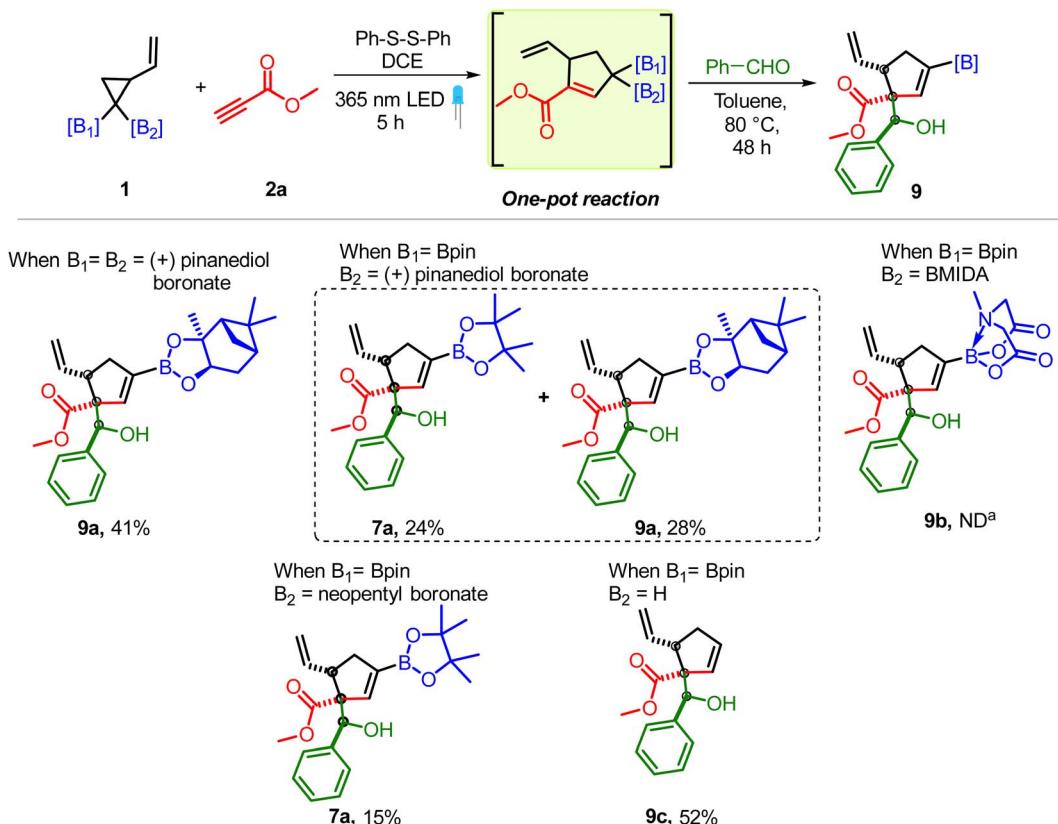
**Scheme 4** Substrate scope of alkynes. Reaction conditions: VCPDB (**1a**, 0.31 mmol), propiolates (**2**, 0.43 mmol, 1.3 equiv.), diphenyl disulfide (0.062 mmol, 20 mol%) and DCE (1.2 mL, 0.25 M), under a 365 nm LED for 5 h followed by DCE removal, addition of aldehyde (0.62 mmol, 2 equiv.) and toluene (1.2 mL, 0.25 M) to the same pot and heating at 80 °C for 48 h. <sup>a</sup> ND = not detected. <sup>b</sup> 1.2 equiv. of diphenyl disulfide and 3 equiv. of alkyne (**5**) were used.

bioactive molecules, alkynes having cholesterol and estrone cores were employed. These reactions successfully provided the corresponding allylboration products (**8j** and **8k**) bearing homoallylic alcohol/ester and steroidal motifs as a single diastereomer. Collectively, the above results demonstrate the benefit of the mild VCPDB-based approach to open up access to unprecedented and structurally complex conjugated allylic diborons and their one-pot conversion into densely functionalized products having contiguous quaternary, tertiary and secondary carbon centers.

To determine the scope of the VCPDB component, vinyl cyclopropanes having (+) pinanediol boronate, MIDA boronate and neopentyl boronate motifs were tested (Scheme 5). The

presence of the geminal bis-pinanediol boronate group or unsymmetrical diboron motif (pinanediol boronate/Bpin and neopentyl boronate/Bpin) on VCP (**1c** and **1e**) allowed the formation of corresponding carbonyl conjugated allylic diboron *via* cycloaddition with **2a** which reacted smoothly with benzaldehyde to give the desired **7a** and **9a** albeit without chirality transfer from (+) pinanediol (Scheme 5). In contrast, VCP having geminal BMIDA/BPin groups didn't participate in the multi-component reaction (**9b**). In addition to the allylic diborons, the formation of carbonyl conjugated monoboronates was also feasible as the VCP containing a single Bpin group (**1f**) led to the desired allylboration product (**9c**). The above results suggest that while one Bpin group ( $sp^2$  – hybridized B) on VCP is





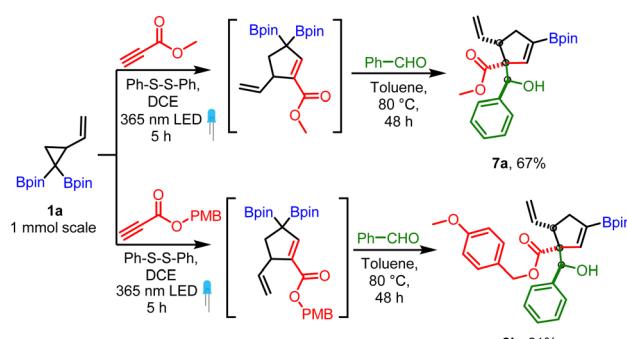
Scheme 5 Substrate scope of vinyl cyclopropanes. Reaction conditions: VCPDB (**1b–1e**, 0.31 mmol), methyl propiolates (**2a**, 0.43 mmol, 1.3 equiv.), diphenyl disulfide (0.062 mmol, 20 mol%) and DCE (1.2 mL, 0.25 M), under a 365 nm LED for 5 h followed by removal of DCE, addition of aldehyde (0.62 mmol, 2 equiv.) and toluene (1.2 mL, 0.25 M) to the same pot and heating at 80 °C for 48 h. <sup>a</sup> ND = not detected.

sufficient to induce the regioselective ring opening of VCP, the presence of a bulky BMIDA group ( $sp^3$  – hybridized B, **9b**) inhibits the VCP ring opening and/or the addition of a homallylic radical (**A**, Scheme 1C) to an alkyne.

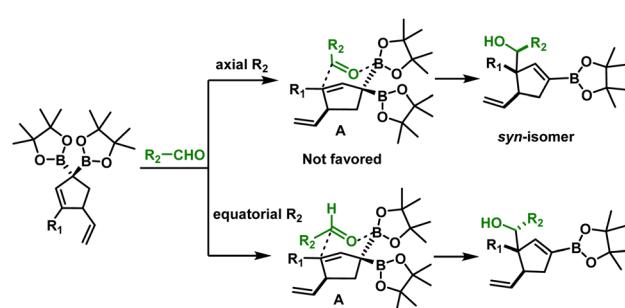
The robustness of the method was confirmed by a scale-up experiment (1 mmol scale) on two different substrates (**7a** and **8b**, Scheme 6). The *anti* diastereoselectivity observed in

allylboration of **3** can be rationalized by the rigid six-membered transition state model<sup>1,22</sup> (Scheme 7) where the aldehyde proton occupies the pseudo axial position. The presence of an allylic diboron motif within the cyclic structure imposes further conformational constraints leading to very high *anti* selectivity.

Our next goal was to establish the synthetic utility of allylboration products (**7–8**). In particular, we wondered if the beta-hydroxy ester motif in **7** or **8** would allow the construction of borylated spiro-fused  $\beta$ -lactone (Scheme 8).  $\beta$ -Lactones are structural frameworks of bioactive natural products and also serve as valuable synthetic intermediates due to inherent strain in the lactone ring.<sup>23–26</sup> In particular, the spiro  $\beta$ -lactones display

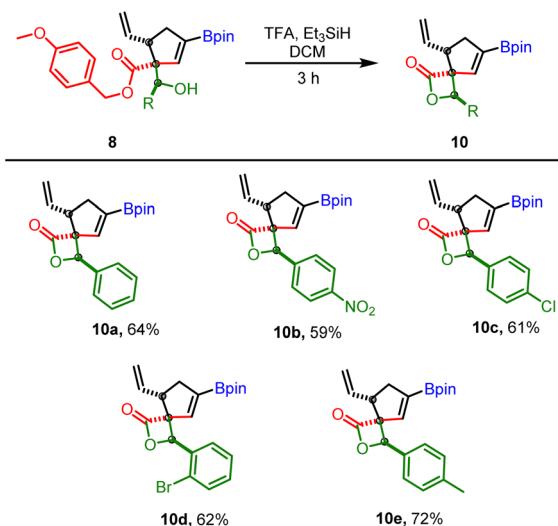


Scheme 6 Scale-up reactions (1 mmol scale); reaction conditions: VCPDB (**1a**, 1 mmol), propiolates (1.3 mmol, 1.3 equiv.), diphenyl disulfide (0.2 mmol, 20 mol%) and DCE (4 mL, 0.25 M), under a 365 nm LED for 5 h followed by removal of DCE and addition of aldehyde (2 mmol, 2 equiv.) and toluene (4 mL, 0.25 M) to the same pot and heating at 80 °C for 48 h.



Scheme 7 Proposed transition state model for allylboration.



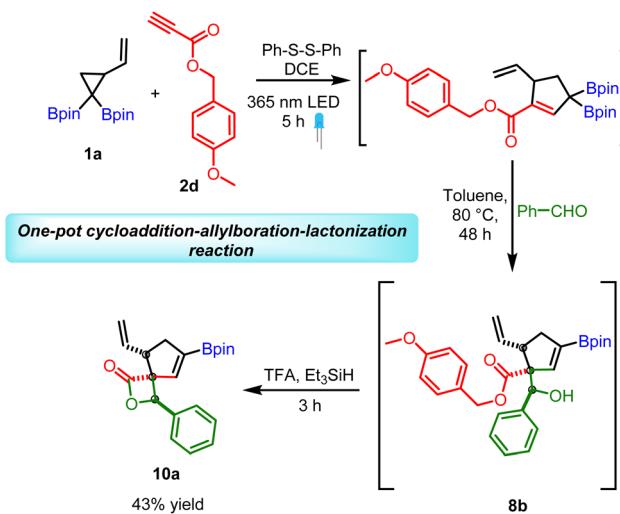


**Scheme 8** Application of allylboration products for spirolactonization; reaction conditions: 8 (0.25 mmol), triethyl silane (2.5 mmol, 10 equiv.) TFA (1.5 mmol, 5 equiv.) in DCM (1 mL, 0.25 M).

potent proteasome inhibitory and GABA antagonistic activity;<sup>27,28</sup> therefore, methods for stereoselective construction of these lactones are in high demand. We reasoned that the allylboration products obtained from *p*-methoxy benzyl (PMB) propiolates could be converted into corresponding  $\beta$ -hydroxy carboxylic acid under mild conditions without disturbing the boronate or vinyl group. This acid could then be activated with BOP-Cl<sup>29</sup> for lactone formation. As a test of this hypothesis, **8b** was treated with BCl<sub>3</sub> for deprotection of PMB ester. To our surprise, instead of the expected acid, the above reaction provided the  $\beta$ -spiro lactone (**10a**) along with some other side products which were difficult to remove by column chromatography. Motivated by the above result, several other acidic conditions for one-pot ester deprotection, spirolactonization, were evaluated.

A combination of trifluoracetic acid (TFA) and Et<sub>3</sub>SiH was found to provide the desired  $\beta$ -spiro lactone in good yield within 3 h (Scheme 8). The substrate scope of this reaction was broad as several other allylboration products containing electron withdrawing groups (nitro, halogen) or electron donating groups (methyl) furnished the bicyclic  $\beta$ -spiro lactone as single diastereomers (Scheme 8). Significantly, the direct conversion of VCPDB (**1a**) into borylated spiro-fused  $\beta$ -lactone was also feasible *via* a one-pot three step reaction (4 C–C bonds formed) with an overall yield (43%, Scheme 9) better than that obtained by two-pot reaction (**10a**, Scheme 8, overall yield = 36%). These results highlight the robustness and versatility of the developed VCPDB-based approach for a concise and stereoselective construction of densely functionalized biologically important molecules containing multiple contiguous stereogenic centers and the synthetically useful vinyl boronate group.

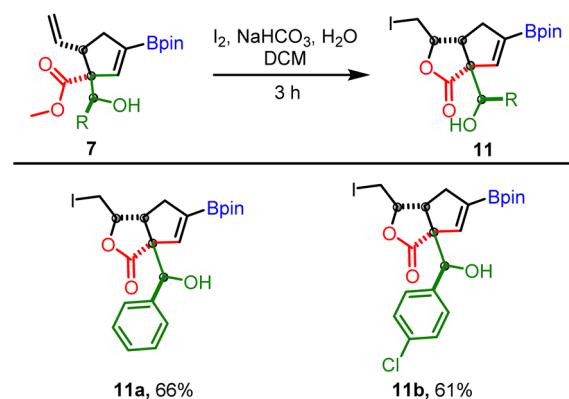
To further demonstrate the utility of allylboration products obtained from conjugated allyl diborons, the *cis*-orientation of  $\beta$ -vinyl and ester groups in **7** was harnessed for iodolactonization reaction. This approach enabled facile access to



**Scheme 9** One-pot tandem cycloaddition–allylboration–lactonization.

bicyclic  $\gamma$ -butyrolactones having a boronate group which can be used for further structural diversification (Scheme 10). It is pertinent to mention that while the  $\gamma$ -butyrolactone<sup>30,31</sup> scaffold is ubiquitous in several bioactive molecules and FDA approved drugs, the exocyclic hydroxyl group present in lactones **11** is also a recurring motif in natural products that regulate antibiotic biosynthesis.<sup>32</sup>

Having established the synthetic utility of conjugated allyl-diborons, mechanistic studies were conducted to better understand the light-promoted thiyl radical catalyzed VCP ring opening and the unusual base-free deboronative allylic shift of **3a**. Based on our previous studies,<sup>20</sup> a plausible mechanism involves the initial generation of thiyl radicals from homolysis of disulfide. This thiyl radical (**I**) adds to the VCPDB (**1**) to give the cyclopropyl carbinyl radical (**II**, Fig. 1A) which can revert back to **1** *via*  $\beta$ -fragmentation or undergo ring opening to form the homoallylic radical (**III**). The presence of a geminal diboron group in **II** favors the ring opening pathway due to the stabilization of the ensuing carbon-centered radical (**III**) *via*



**Scheme 10** Application of allylboration products for iodolactonization. Reaction conditions: 7 (0.25 mmol), iodine (0.3 mmol, 1.2 equiv.), NaHCO<sub>3</sub> (0.3 mmol, 1.2 equiv.), H<sub>2</sub>O (200  $\mu$ L) in DCM (1 mL, 0.25 M).



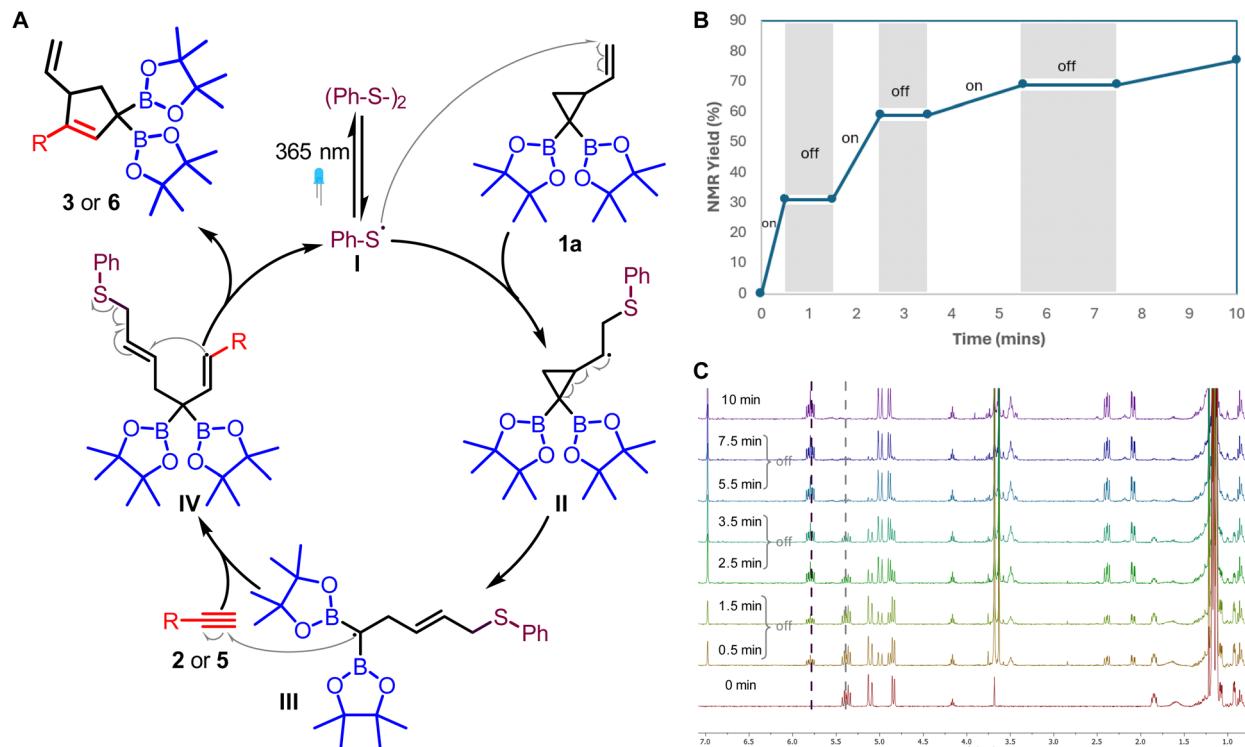


Fig. 1 (A) A plausible mechanism for [3 + 2] radical cycloaddition; (B) light "on/off" experiment; (C) stacked <sup>1</sup>H NMR from "on/off" experiments at different time intervals.

conjugation with the empty p-orbitals of two boron atoms. The homoallylic radical (**III**) undergoes addition to an alkyne which is followed by ring closure and concomitant regeneration of the

thiy radical. Light-on/off experiments indicated the need for continuous irradiation of the reaction mixture (Fig. 1B). This result suggests that the thiy radical released from the catalytic

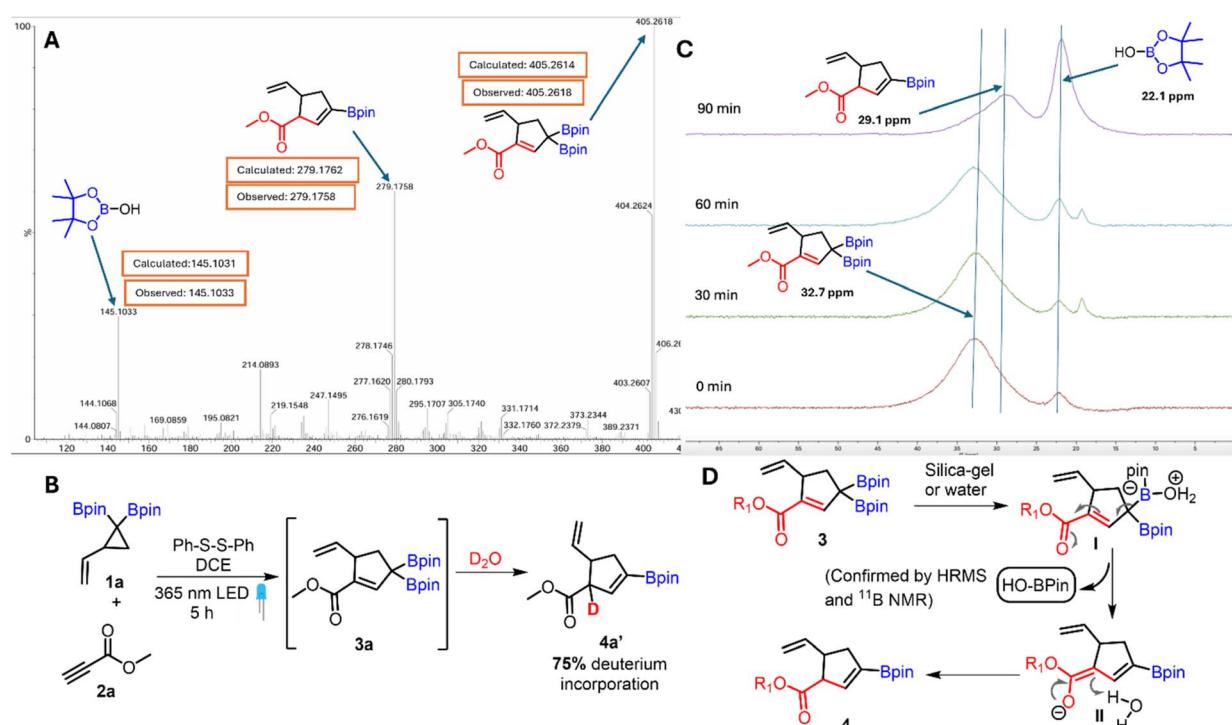


Fig. 2 Mechanistic studies of the base-free deboronative allylic shift. (A) HRMS analysis of carbonyl conjugated allylic diboron. (B) Deuterium labeling experiment. (C) <sup>11</sup>B NMR analysis of silica-gel induced deboronation. (D) Proposed mechanism.

cycle participates in two competing pathways: recombination to give the disulfide or addition to VCPDB (**1**).

The High Resolution Mass Spectrum (HRMS) of crude **3a** using the ASAP probe showed the presence of **3a**, vinyl boronate **4a** and the Bpin-OH species (Fig. 2A) which indicates deboronation during the mass spec analysis. The deuterium labelling experiment performed by treating **3a** in D<sub>2</sub>O showed 75% deuterium incorporation at the alpha-position of the ester (Fig. 2B).

The silica-gel mediated deboronation was monitored by <sup>11</sup>B NMR spectroscopy (Fig. 2C) in CDCl<sub>3</sub> as solvent. During the first few minutes of this experiment, the allyl boron was the major species ( $\delta = 32.7$  ppm); however, the intensity of this signal progressively decreased with a concomitant increase in the intensity of the resonance at  $\delta = 29.1$  and 22.1 ppm which was assigned to vinyl boronate and Bpin-OH<sup>33</sup> byproducts respectively. Similar <sup>11</sup>B NMR spectral data was obtained when silica gel was replaced with water (see the ESI<sup>†</sup>). In view of the above data, a plausible mechanism (Fig. 2D) involves coordination of water molecules with the BPin to generate the boronate complex (**I**). The presence of an  $\alpha,\beta$ -unsaturated ester motif in this intermediate induces water mediated deboronation resulting in the formation of dienolate (**II**) which undergoes protonation to afford the vinyl boronate (**4**).

## Conclusion

In conclusion, this work discloses the first examples of carbonyl conjugated allylic boronates and metal-free one-pot formation-nucleophilic addition of allylic boronates. A photocatalytic [3 + 2] cycloaddition of vinyl cyclopropyl boronates (VCPDB) with propiolates provided highly substituted allyldiboronates conjugated to an ester group. This mild base- and transition metal-free approach enabled a tandem cycloaddition–allylboration reaction involving an *in situ* formation of allyl boronates followed by their nucleophilic addition to aldehydes. The above one-pot multicomponent reaction showed broad substrate scope and excellent diastereoselectivity to afford highly functionalized borylated homoallylic alcohols featuring the  $\beta$ -hydroxy ester and  $\beta$ -vinyl ester motifs across contiguous quaternary, tertiary and secondary stereogenic centers. These unique allylboration products opened up access to other rare and congested alkenyl borons such as borylated spiro-fused  $\beta$ -lactones and bicyclic  $\gamma$ -butyrolactones which are components of bioactive molecules. Of note, the direct conversion of VCPDB into spiro  $\beta$ -lactones *via* a one-pot three step process was also feasible. The carbonyl conjugated allylic boronates also displayed an unexpected deboronative allylic shift reaction in the presence of silica gel or water. Detailed mechanistic studies involving <sup>11</sup>B NMR, deuterium labelling and mass spec analysis suggested the involvement of a dienolate intermediate *via* water-mediated deboronation.

## Data availability

The data that support the findings of this study are available within the article and its ESI<sup>†</sup>. Crystallographic data for

compounds **4a** and **7h** are available free of charge from the Cambridge Crystallographic Data Centre under references CCDC 2377383 and 2377384. All other data are available in the main text or the ESI.<sup>†</sup>

## Author contributions

A. S. and H. V. designed the research. A. S., H. V., A. G. and A. M. analyzed the data. H. V., A. G., A. M., M. P., A. R. conducted the experiments. A. S. wrote the manuscript with input from all the coauthors.

## Conflicts of interest

The authors declare no competing financial interests.

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