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Organocatalytic reductive coupling of aldehydes with 1,1-diarylethylenes using an *in situ* generated pyridine-boryl radical†

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A pyridine-boryl radical promoted reductive coupling reaction of aldehydes with 1,1-diarylethylenes has been established *via* a combination of computational and experimental studies. Density functional theory calculations and control experiments suggest that the ketyl radical from the addition of the pyridine-boryl radical to aldehydes is the key intermediate for this C–C bond formation reaction. This metal-free reductive coupling reaction features a broad substrate scope and good functional compatibility.

Introduction

Carbon–carbon bond formation is the most important transformation in organic synthesis.¹ The catalytic reductive coupling of olefins with carbonyl compounds is one of the most economical C–C bond constructing methods, due to the abundant source of olefins and carbonyl compounds.² Traditionally, transition metal catalysts have played privileged roles in these transformations, including metal-catalyzed C=O reductive coupling (Scheme 1, top)^{3–5} and redox-triggered C=O coupling *via* H₂ transfer (Scheme 1, middle).⁴ However, sensitive organometallic reagents or transition-metal catalysts are usually required in these reactions. In contrast, organocatalytic reductive coupling of olefins with carbonyl derivatives for C–C bond formation in the presence of sensitive functional groups or congested structural environments is still rare.^{5d}

Boron containing radicals are important reactive intermediates in organic synthesis.^{6–13} In this context, our group recently revealed that the pyridine-ligated boryl radical (Py-Bpin[•]) could be readily generated from (pinacolato)diboron (B₂pin₂) through a cooperative catalysis involving two 4-cyanopyridine molecules.¹¹ This kind of pyridine-boryl radical was used for the catalytic reduction of azo-compounds¹¹ or as a carbon-centered radical for the synthesis of 4-substituted

pyridines.¹² Moreover, the pyridine-boryl radical can act as a persistent radical¹³ for the synthesis of organoboronate derivatives.¹⁴ Because the precursors (pyridines and B₂pin₂) of these pyridine-boryl radicals are inexpensive and stable,¹⁵ the development of new chemical transformations with these pyridine-boryl radicals is attractive. In this work, we further explored pyridine-boryl radical chemistry in the organocatalytic reductive coupling of aldehydes with 1,1-diarylethylenes (Scheme 1, bottom), which, to the best of our knowledge, has not been reported previously.

Results and discussion

It will be shown that the reductive coupling of aldehydes and olefins can be promoted by an *in situ* generated pyridine-boryl radical, following the proposed pathway as shown in Scheme 2. The proposed catalytic cycle consists of the following four steps: (1) activation of the B–B bond of B₂pin₂ by pyridines to form a pyridine-boryl radical (**Int1**); (2) the addition of the pyridine-boryl radical to aldehyde **1a** to generate a new ketyl radical (**Int3**), with the regeneration of the pyridine catalyst; (3) the

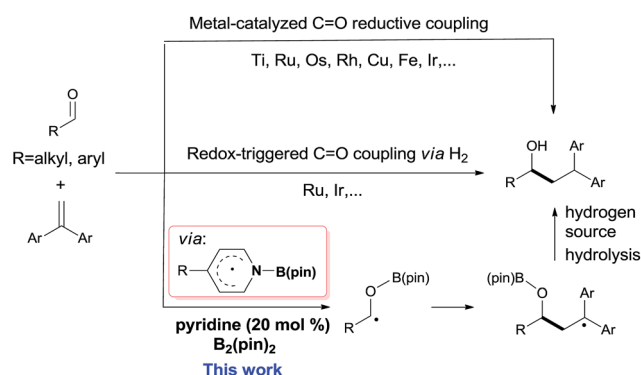
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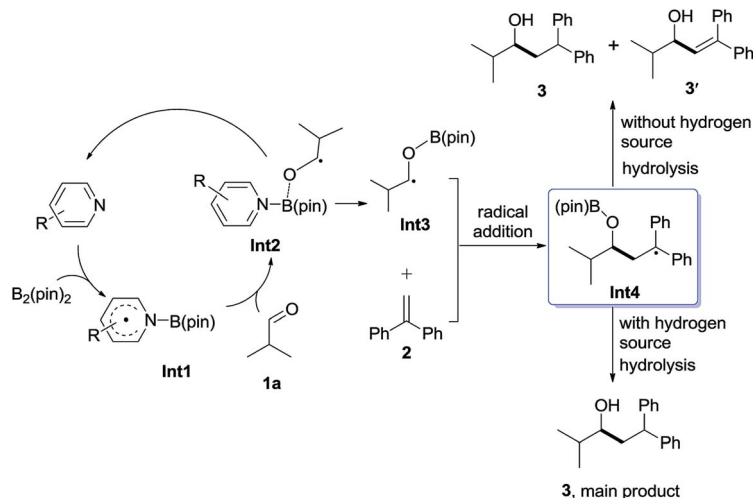
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‡ These authors contributed equally to this work.



Scheme 1 Reductive coupling of carbonyl compounds with olefins.





Scheme 2 Proposed mechanism for the reductive coupling of isobutyraldehyde and 1,1-diphenylethylene.

addition of the new ketyl radical to 1,1-diphenylethylene to yield a diaryl-stabilized radical species (**Int4**); and (4) the hydrogen abstraction of **Int4** from an appropriate H-source to yield the final reductive coupling product. In addition, one molecule of **Int4** may also abstract a hydrogen atom from another molecule of **Int4** to give the reductive coupling product and another disproportionation product. To make this catalytic cycle happen, it is necessary to inhibit the possible radical-radical C–C coupling reaction between the pyridine-boryl radical and the ketyl radical, as observed between α,β -unsaturated ketones and 4-cyanopyridine in the presence of B₂pin₂.¹² Thus, other pyridines with different substituents may be better catalysts than 4-cyanopyridine for the proposed reaction. With a pyridine-boryl radical bearing a suitable substituent, its reactivity might be tuned so that the newly generated ketyl radical could react with 1,1-diphenylethylene to yield a diaryl-stabilized radical species, which then undergoes a hydrogen atom abstraction from an appropriate hydrogen source to produce the reductive coupling product.

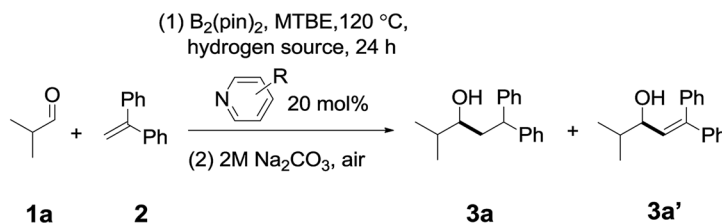
To find suitable pyridines which can react with B₂pin₂ to form the corresponding pyridine-boryl radical under mild conditions, we first performed density functional theory (DFT) calculations with the M06-2X¹⁶ functional to screen a series of pyridines. A careful analysis of stationary points revealed that the formation of the pyridine-boryl radical proceed through a [3,3]-sigmatropic rearrangement/homolytic C–C bond cleavage pathway¹⁷ rather than *via* the direct homolytic cleavage of the B–B bond^{14,18} (see Fig. S1 and S2 in the ESI† for details). As shown in Fig. S1–S12,† the [3,3]-sigmatropic rearrangement is the rate-determining step for the formation of the corresponding pyridine-boryl radical. The activation barrier of this step with different pyridines is highly dependent on the substituent in the pyridine ring. Pyridines with an electron-withdrawing group at the C4 position, such as CN (**A**), 4-cyano phenyl (**B**), Ph (**C**), and CF₃ (**D**), have lower barriers than unsubstituted pyridines and pyridines with an electron-donating group (CH₃, CH₃O, and N(CH₃)₂). The pyridine with a CF₃ group at the C3

position has a slightly higher activation barrier than that with the same group at the C4 position (**D** > **E**). These results indicate that the activation barrier of pyridines correlates closely with the resonance effect and the inductive effect of the substituents. According to the calculated activation barriers, five pyridines (**A**, **B**, **C**, **D**, and **E**) with barriers of no more than 28.5 kcal mol^{−1} are possible candidates for cleaving the B–B bond of B₂pin₂.

In order to determine a suitable combination of a pyridine catalyst and a hydrogen source, we conducted an initial investigation on the reaction between isobutyraldehyde **1a** and 1,1-diphenylethylene **2** (see Tables S1 to S3† for details). As shown in Table 1, by heating a mixture of isobutyraldehyde **1a** (1.0 equiv.), 1,1-diphenylethylene (2.0 equiv.), and B₂pin₂ (1.0 equiv.) in the presence of 1,3,5-trimethyl-1,4-cyclohexadiene (a hydrogen source, 1.0 equiv.) and 4-cyanopyridine **A** (0.2 equiv.) in *tert*-butyl methyl ether (MTBE) at 120 °C, the desired reductive coupling product **3a** was observed in 28% yield (entry 1), together with a small amount of pyridine-aldehyde adducts (12% yield, see the ESI† for details). When 4-(4-pyridinyl)benzotrile **B** was used as the catalyst (entry 2), the NMR yield of **3a** improved to 78%, and the yield of a byproduct **3a'** from the disproportionation of the diaryl radical intermediate (**Int4**) was 6%. However, when other pyridines (for example **C**, **D**, or **E**, entries 3–5) were adopted, the yield of **3a** decreased significantly. If Et₃SiH was chosen as the hydrogen source, the yield of **3a** is somewhat lower than that with 1,3,5-trimethyl-1,4-cyclohexadiene as a hydrogen source (entry 6). In the absence of a hydrogen source (entry 7), the ratio of **3a/3a'** was 52% : 16%, suggesting that the addition of a hydrogen source is important for improving the yield of **3a** (see Table S2†).

Under the optimum conditions (Table 1, entry 2), we explored the generality of this transformation with a series of alkyl and aryl aldehydes. As shown in Table 2, the reductive coupling reactions of several fully aliphatic aldehydes proceeded with good efficiency (**1a–1d**). It was noteworthy that aldehydes with C=C double bond (**1e**), methylthio (**1f**), or furyl (**1h**) functionalities on the alkyl chain were tolerated, giving the



Table 1 Optimization of the reaction conditions^a

Entry	Hydrogen source	Pyridines with different <i>R</i> substituents	Ratio [3a / 3a'] ^b
1	TMe-1,4-CHD	4-CN (A)	28% : 0%
2	TMe-1,4-CHD	4-(4-Cyanophenyl) (B)	78% : 6% (70%) ^c
3	TMe-1,4-CHD	4-Ph (C)	16% : 2%
4	TMe-1,4-CHD	4-CF ₃ (D)	21% : 1%
5	TMe-1,4-CHD	3-CF ₃ (E)	0%
6	Et ₃ SiH	4-(4-Cyanophenyl) (B)	62% : 16%
7	—	4-(4-Cyanophenyl) (B)	52% : 16%

^a Reaction conditions: isobutyraldehyde (0.2 mmol), $B_2(\text{pin})_2$ (0.2 mmol), catalyst (0.04 mmol), 1,1-diphenylethylene (0.4 mmol), H-donor (0.2 mmol), 24 hours, 120 °C, and MTBE (1 mL). ^b Yields were determined by ¹H-NMR analysis of the crude mixture using CH_2Br_2 as the internal standard. ^c Isolated yield of **3a**. TMe-1,4-CHD = 1,3,5-trimethyl-1,4-cyclohexadiene.

reductive coupling products in moderate to good yields. The α -branched aldehydes (**1i–1r**), in particular, pivaldehyde (**1q**) and 1-adamantylcarboxaldehyde (**1r**), also reacted well to afford the desired products in good yields. It should be mentioned that the substrates with a congested structure environment show less reactivity in transition-metal catalyzed reductive coupling of olefins and aldehydes, possibly because the coordination between the metal centre and the corresponding substrates is difficult.^{4c} However, our method is also suitable for butyl aldehydes (**1q** and **1r**). Beside alkyl aldehydes, aryl aldehydes (**1s** and **1t**) bearing electron-donating groups (CH_3 and CH_3O) could also serve as the coupling partners, furnishing corresponding products in moderate yields. In addition to aldehydes, alkyl ketones (**1u–1w**) also reacted smoothly to provide the desired alcohols in 27–42% yield.

Diarylalkanes are important pharmacophores in drugs.¹⁹ It would be attractive to apply this metal-free method in the late stage functionalization of medicinally related molecules. As shown in Table 2(C), an abietic acid derivative (**1x**) and gemfibrozil derivative (**1y**) reacted smoothly with 1,1-diphenylethylene to form **3x** and **3y** in acceptable yields, respectively.

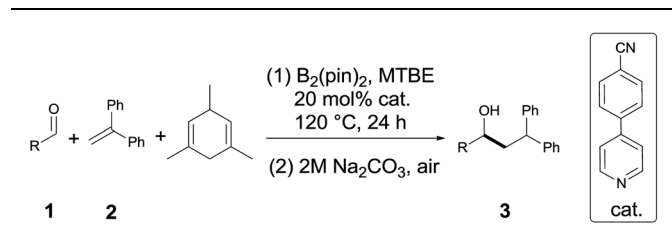
Next, the scope of 1,1-diarylalkenes (**4**) was examined (Table 3(a)). Both symmetrical (**4a–d**) and unsymmetrical (**4e–o**) 1,1-diarylalkenes were converted into the corresponding products **5** in moderate to good yields with modest diastereoselectivities. The reaction tolerated substrates bearing various functional groups on the benzene ring, such as halogen functionalities (**4c** and **4d**), CF_3 (**4e**), CN (**4f** and **4g**), MeO (**4h**), CH_3S (**4i**), CO_2Me (**4j**), and *t*Bu (**4k**). More importantly, 1,1-diarylalkenes containing heterocyclic structures (**4m–o**), such as benzofuran (**4o**) and thioxanthene (**4p**), also reacted smoothly to give the expected products in reasonable yields. Additionally, we also tested the reactivity of other alkenes with pivaldehyde **1q** (Table 3(b)).

However, our results show that other alkenes, including ethyl 2-phenylacrylate (**4q**), styrenes (**4r** and **4s**) or aliphatic olefin (**4t**), generally gave little or no desired product. The reason why 1,1-diarylalkenes are suitable coupling partners of ketyl radicals may be due to (1) the radical stabilization effect of two aryl groups, and (2) the less nucleophilicity of present boron-ketyl radicals (compared with typical ketyl radicals).^{5b} Thus, this protocol provides a metal-free reductive coupling method of 1,1-diarylalkenes with aldehydes (*via* the radical addition mechanism), which traditionally requires transition metal catalysts or organometallic reagents.^{12–16}

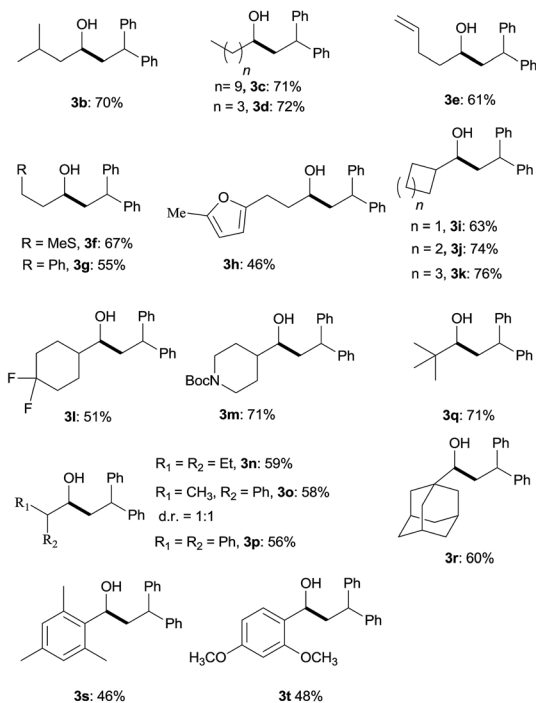
To understand the mechanism of the reductive coupling of 1,1-diarylalkenes with aldehydes, we have performed DFT calculations with the M06-2X functional to explore the free energy profile of the proposed mechanism for the reaction between isobutyraldehyde (**1a**) and 1,1-diphenylethylene (**2**) in the presence of **Int1** as a reactive intermediate. Our theoretical studies have shown that the generation of **Int1** from $B_2\text{pin}_2$ and 4-(4-pyridinyl)benzotrile is exergonic by 13.4 kcal mol⁻¹ (see Fig. S4†). The calculated free energy profile and transition state structures are displayed in Fig. 1 (the optimized structures of all minimum species are shown in Fig. S12†). First, the coordination of the oxygen atom of isobutyraldehyde to the boron atom of the pyridine-boryl radical **Int1** generates a boron-containing intermediate (**Int2**) *via* **TS1**, with a barrier of 13.3 kcal mol⁻¹. Then, the breaking of the B–N bond in **Int2** yields a ketyl radical (**Int3**) and regenerates the 4-(4-pyridinyl)benzotrile catalyst. This process is exothermic by 4.5 kcal mol⁻¹, with a barrier of 3.2 kcal mol⁻¹ (relative to **Int2**), suggesting that the formation of the ketyl radical (**Int3**) from **Int2** is possible. Next, the addition of **Int3** to the β -position of 1,1-diphenylethylene to form a diaryl-stabilized radical (**Int4**) *via* **TS3** is exothermic by 15.6 kcal mol⁻¹, with a barrier of 15.5



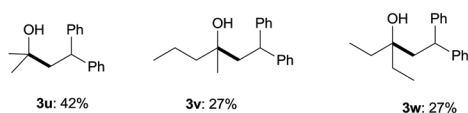
Table 2 Substrate scope for the reductive coupling of aldehydes or ketones with 1,1-diphenylethylene^a



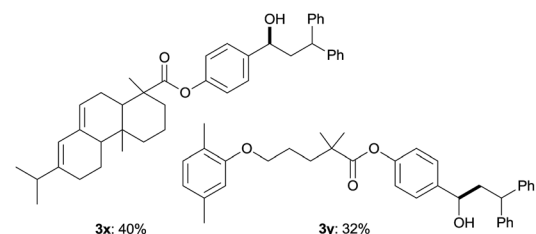
A. aldehydes



B. ketones



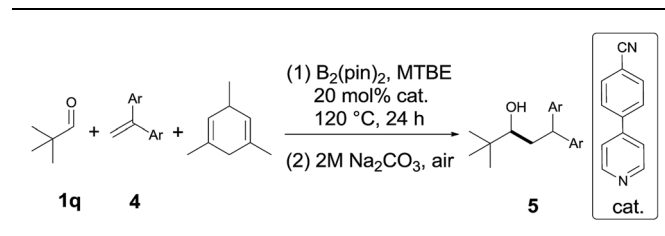
C. late stage functionalization of medicinally related molecules



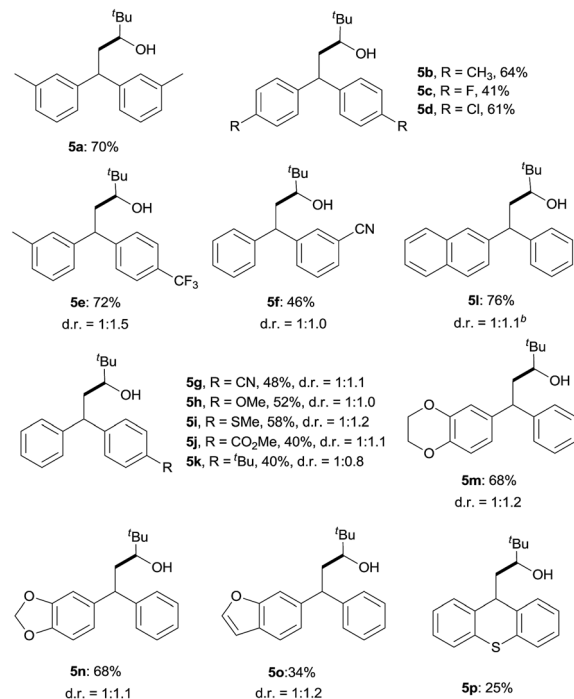
^a Reaction conditions: aldehyde (0.2 mmol), B₂(pin)₂ (0.2 mmol), 4-(4-pyridinyl)benzotrile (0.04 mmol), 1,1-diphenylethylene (0.4 mmol), 1,3,5-trimethyl-1,4-cyclohexadiene (0.2 mmol), MTBE (1.0 mL), 24 h, and 120 °C. Isolated yield. The diastereoselectivities (d. r.) were determined by ¹H-NMR analysis of the crude mixture. Boc = *tert*-butoxycarbonyl.

kcal mol⁻¹ (with respect to the radical **Int3**). Finally, the final product is obtained with a hydrogen atom abstraction from 1,3,5-trimethyl-1,4-cyclohexadiene *via* **TS4** with a barrier of

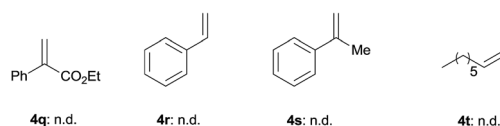
Table 3 Substrate scope for the reductive coupling of pivaldehyde with 1,1-diarylethylenes^a



(a) 1,1-diarylethylenes



(b) other alkenes



^a Reaction conditions: pivaldehyde (0.2 mmol), B₂(pin)₂ (0.2 mmol), 4-(4-pyridinyl)benzotrile (0.04 mmol), 1,1-diarylethylene (0.4 mmol), 1,3,5-trimethyl-1,4-cyclohexadiene (0.2 mmol), MTBE (1.0 mL), 24 h, and 120 °C. Isolated yield. The diastereoselectivities (d. r.) were determined by ¹H-NMR analysis of the crude mixture. ^b The diastereoselectivities (d. r.) were determined by GC-MS analysis of the crude mixture. ^tBu = *tert*-butyl.

26.3 kcal mol⁻¹ (relative to the radical **Int4**). The whole reductive coupling reaction is exergonic by 11.7 kcal mol⁻¹ (with respect to the reactants **1a** and **Int1**). These results suggest that the studied reaction is thermodynamically and kinetically feasible under the experimental conditions. In addition, our calculations suggest that the direct single electron transfer (SET) process between the pyridine-boryl radical and isobutyraldehyde is highly endergonic (see details in Fig. S13 and S14[†]). Thus, the SET mechanism for the present reaction can be excluded.



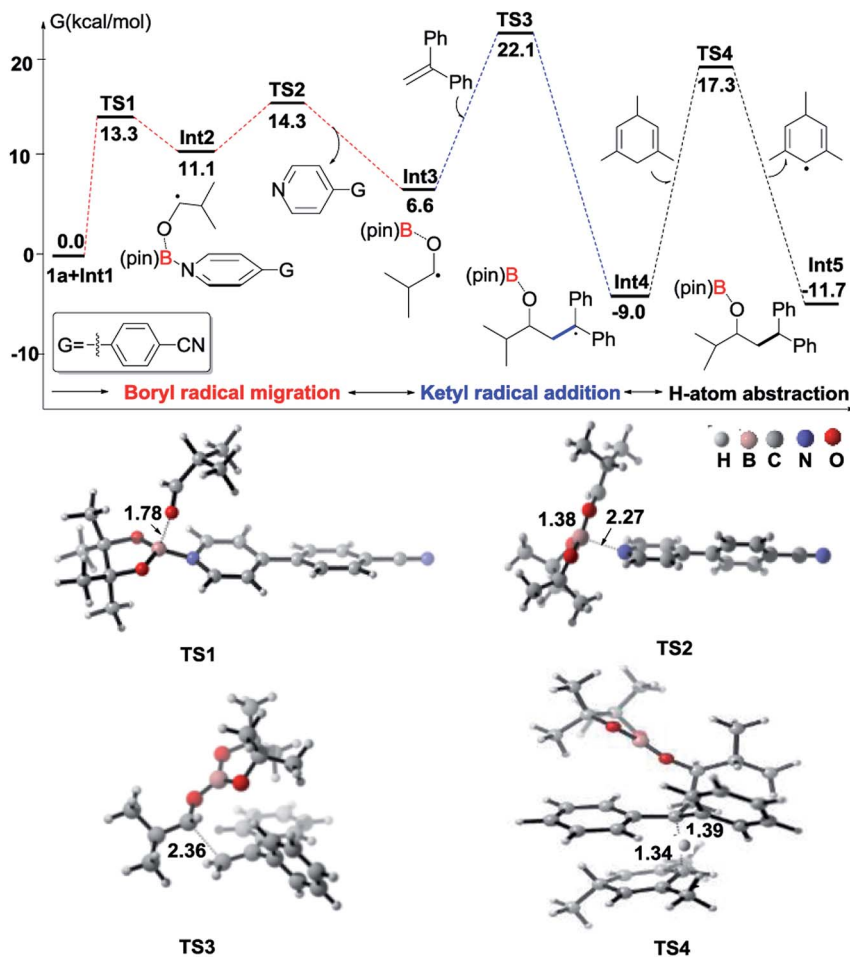
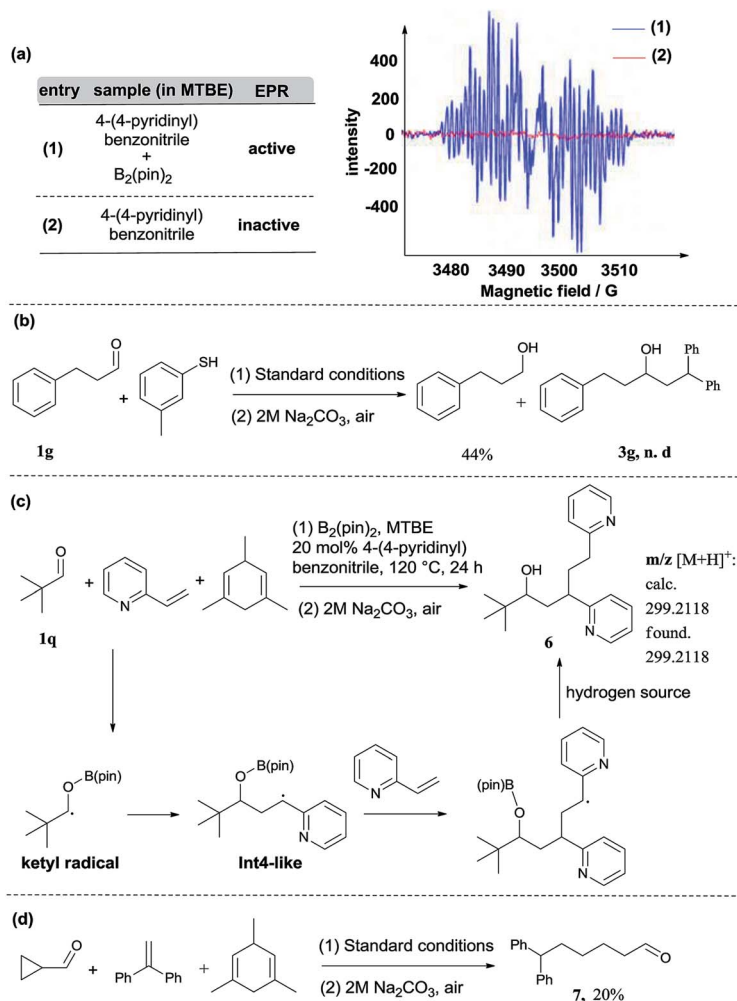


Fig. 1 Computed Gibbs free energy profile of the reductive coupling reaction between isobutyraldehyde (**1a**) and 1,1-diphenylethylene (**2**) promoted by the 4-(4-pyridinyl)benzotrile-boryl radical (**Int1**). The optimized structures of transition states in the reaction path are also displayed. Interatomic distances are in Å.

In addition to DFT calculations described above, we also conducted several experiments to verify the proposed pathway. First, the EPR signal was observed for the reaction of 4-(4-pyridinyl)benzotrile and $B_2(\text{pin})_2$, which supports the formation of the proposed pyridine-boryl radical, as shown in Scheme 3a. Second, the involvement of the ketyl radical was confirmed by a competition experiment (Scheme 3b). It has been reported that thiols are quick hydrogen atom donors that can interfere with the radical reaction.²⁰ When the hydrogen source 1,3,5-trimethyl-1,4-cyclohexadiene was replaced by 3-methylbenzenethiol, the ketyl radical quickly abstracted a hydrogen atom from 3-methylbenzenethiol to yield the reductive product, 3-phenyl-1-propanol, so that its addition to 1,1-diphenylethylene (to form the reductive coupling product) was inhibited (see Page S20[†]). This result clearly indicated the involvement of the ketyl radical. Third, the generation of the radical species **Int4** (or its analogues) *via* the addition of the ketyl radical to the β -position of aryethylene was confirmed by an intermolecular trapping experiment (Scheme 3c). When 2-vinylpyridine and trimethylacetaldehyde were subjected to the standard reaction conditions, species **6** could be detected by HRMS analysis for the crude reaction mixture (see Page S21[†]).

This result suggests that in this reaction, the radical species **Int4-like** was further trapped by another 2-vinylpyridine molecule. However, in the presence of 2-vinylpyridine as a substrate, the yield of **6** is quite low and its isolation from the reaction mixture was not successful. Besides, we further conducted analysis of the ^{11}B -NMR spectrum and HRMS to detect the formation of the proposed O-boron intermediate (**Int6**, Fig. S17[†]). The ^{11}B -NMR of the crude reaction mixture displays resonances at ~ 21 ppm, which is consistent with the signal of a boron atom bound to three oxygen atoms.²¹ In addition, our HRMS analysis (with 4-vinylpyridine as the substrate) also indicates the formation of the O-boron intermediate (**Int7**), as shown in Fig. S18.[†] Moreover, we have performed a radical-clock study using cyclopropanecarboxaldehyde as the substrate. The experimental results indicate that some ketyl radicals first convert into the corresponding carbon radicals (*via* a ring-opening process) and then add to the alkene to form the ring-opening product (Scheme 3d). The experiments described above provide strong evidence on the involvement of a radical addition step between the ketyl radical and 1,1-diarylethylene in this reaction.





Scheme 3 Controlled experiments.

Conclusions

In summary, we have established the organocatalytic reductive coupling of aldehydes with 1,1-diaryllkenes *via* a combination of computational and experimental studies. This study showed that 4-(4-pyridinyl)benzonitrile is a suitable catalyst for cleaving the B–B bond of B₂pin₂, and the ketyl radical from the addition of an *in situ* generated pyridine-boryl radical to aldehydes is a key intermediate for the C–C bond formation. The reaction is practical and applicable to a broad range of aldehydes and 1,1-diaryllkenes with good functional group tolerance. DFT calculations and control experiments were conducted to verify the proposed mechanism. This pyridine-boryl radical promoted radical addition mechanism represents a metal-free reductive coupling reaction of aldehydes with 1,1-diaryllkenes. Further studies will be directed toward the development of new transformations involving readily formed pyridine-boryl radicals with the aid of combined theoretical and experimental studies.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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Notes and references

- (a) M. Fagnoni, D. Dondi, D. Ravelli and A. Albini, *Chem. Rev.*, 2007, **107**, 2725; (b) C. L. Sun and Z. J. Shi, *Chem. Rev.*, 2014, **114**, 9219.
- (a) B. Sam, B. Breit and M. J. Krische, *Angew. Chem., Int. Ed.*, 2015, **54**, 3267; (b) K. D. Nguyen, B. Y. park, T. Luong, H. Sato, V. J. Garza and M. J. Krische, *Science*, 2016, **354**, 6310; (c) S. W. Kim, W. Zhang and M. J. Kriche, *Acc. Chem. Res.*, 2017, **50**, 2371.
- (a) M. Kimura, A. Ezoe, K. Shibata and Y. Tamaru, *J. Am. Chem. Soc.*, 1998, **120**, 4033; (b) J. A. Marshall and N. D. Adamas, *J. Org. Chem.*, 1998, **63**, 3812; (c)



- J. A. Marshall and N. D. Adamas, *J. Org. Chem.*, 1999, **64**, 5201; (d) J. A. Marshall and H. R. Chobanian, *J. Org. Chem.*, 2000, **65**, 8357; (e) H. Y. Jang, R. R. Huddleston and M. J. Krische, *J. Am. Chem. Soc.*, 2002, **124**, 15156; (f) J. F. Bower, R. L. Patman and M. J. Krische, *Org. Lett.*, 2008, **10**, 1033; (g) I. S. Kim, M.-Y. Ngai and M. J. Krische, *J. Am. Chem. Soc.*, 2002, **124**, 12156; (h) C. C. Wang, P. S. Lin and C. H. Cheng, *J. Am. Chem. Soc.*, 2002, **124**, 9696; (i) L. M. Geary, S. K. Woo, J. C. Leung and M. J. Krische, *Angew. Chem., Int. Ed.*, 2012, **51**, 2972; (j) L. M. Geary, J. C. Leung and M. J. Krische, *Chem.-Eur. J.*, 2012, **18**, 16823.
- 4 (a) S. Y. Zhang, Y. Q. Tu, C. A. Fan, F. M. Zhang and L. Shi, *Angew. Chem., Int. Ed.*, 2009, **48**, 8761; (b) J. M. Ketcham, I. Shin, T. P. Montgomery and M. J. Krische, *Angew. Chem., Int. Ed.*, 2014, **53**, 9142; (c) Y. L. Zheng, Y. Y. Liu, Y. M. Wu, Y. X. Wang, Y. T. Lin and M. Ye, *Angew. Chem., Int. Ed.*, 2016, **55**, 6315.
- 5 (a) M. Nakajima, E. Fava, S. Loescher, Z. Jiang and M. Rueping, *Angew. Chem., Int. Ed.*, 2015, **54**, 8828; (b) L. Qi and Y. Chen, *Angew. Chem., Int. Ed.*, 2016, **55**, 13312; (c) K. N. Lee, Z. Lei and M.-Y. Ngai, *J. Am. Chem. Soc.*, 2017, **139**, 5003; (d) L. Pitzer, F. Sandfort, F. Strieth-Kalthoff and F. Glorius, *J. Am. Chem. Soc.*, 2017, **139**, 13652.
- 6 (a) B. P. Roberts, *Chem. Soc. Rev.*, 1999, **28**, 25; (b) B. Carboni and L. Monnier, *Tetrahedron*, 1999, **55**, 1197; (c) C. Ollivier and P. Renaud, *Chem. Rev.*, 2001, **101**, 3415; (d) *Radicals in Organic Synthesis*, ed. P. Renaud and M. P. Sibi, Wiley-VCH, Weinheim, 1st edn, 2001, pp. 11–27; (e) P. P. Power, *Chem. Rev.*, 2003, **103**, 789; (f) P. Renaud, A. Beauseigneur, A. Brecht-Forster, B. Becattini, V. Darmency, S. Kandhasamy, F. Montermini, C. Ollivier, P. Panchaud, D. Pozzi, E. M. Scscanlan, A.-P. Schaffner and W. Weber, *Pure Appl. Chem.*, 2007, **79**, 223; (g) D. Crich, D. Grant, V. Krishnamurthy and M. Patel, *Acc. Chem. Res.*, 2007, **40**, 453; (h) A. Staubitz, A. P. M. Robertson, M. E. Sloan and I. Manners, *Chem. Rev.*, 2010, **110**, 4023; (i) D. Lu, C. Wu and P. Li, *Chem.-Eur. J.*, 2014, **20**, 1630; (j) A. Martí-Sómer, O. Mó and M. Yáñez, *ChemPhysChem*, 2014, **15**, 2288; (k) M. Yan, J. C. Lo, J. T. Edwards and P. S. Baran, *J. Am. Chem. Soc.*, 2016, **138**, 12692; (l) D. Zhao and Z. Xie, *Angew. Chem., Int. Ed.*, 2016, **55**, 3166.
- 7 For selected examples on N-heterocyclic carbene-boryl radical, see: (a) S. H. Ueng, M. M. Brahmi, É. Derat, L. Fensterbank, E. Lacôte, M. Malacria and D. P. Curran, *J. Am. Chem. Soc.*, 2008, **130**, 10082; (b) J. C. Walton, M. M. Brahmi, L. Fensterbank, E. Lacôte, M. Malacria, Q. Chu, S. H. Ueng, A. Solovjev and D. P. Curran, *J. Am. Chem. Soc.*, 2010, **132**, 2350; (c) J. C. Walton, M. M. Brahmi, J. Monot, L. Fensterbank, M. Malacria, D. P. Curran and E. Lacôte, *J. Am. Chem. Soc.*, 2011, **133**, 10312; (d) X. Pan, A. L. Vallet, S. Schweizer, K. Dahbi, B. Delpech, N. Blanchard, B. Graff, S. J. Geib, D. P. Curran, J. Lalevée and E. Lacôte, *J. Am. Chem. Soc.*, 2013, **135**, 10484; (e) T. Kawamoto, S. J. Geib and D. P. Curran, *J. Am. Chem. Soc.*, 2015, **137**, 8617; (f) G. Tambutet and Y. Guindon, *J. Org. Chem.*, 2016, **81**, 11427; (g) S. C. Ren, F. L. Zhang, J. Qi, Y. S. Huang, A. Q. Xu, H. Y. Yan and Y. F. Wang, *J. Am. Chem. Soc.*, 2017, **139**, 6050; (h) M. F. Silva, P. Schweyen, D. Gisinger, T. Bannenberg, M. Freytag, C. Kleeberg and M. Tamm, *Angew. Chem., Int. Ed.*, 2017, **56**, 1135; (i) J. W. Taylor, A. M. Skimming, C. F. Guzman and W. H. Will, *J. Am. Chem. Soc.*, 2017, **139**, 11032.
- 8 For selected examples on the amine-boryl radical, see: (a) J. A. Baban, V. P. J. Marti and B. P. Robert, *J. Chem. Soc., Perkin Trans. 2*, 1985, 1723; (b) K. M. Johnson, J. Nicholas Kirwan and B. P. Robert, *J. Chem. Soc., Perkin Trans. 2*, 1990, 1125; (c) J. Lalevée, N. Blanchard, A. C. Chany, M. A. Tehfe, X. Allonas and J.-P. Fouassier, *J. Phys. Org. Chem.*, 2009, **22**, 986; (d) J. Lalevée, N. Blanchard, M. A. Tehfe, A. C. Chany and J. P. Fouassier, *Chem.-Eur. J.*, 2010, **16**, 12920; (e) Y. Aramaki, H. Omiya, M. Yamashita, K. Nakabayashi, S. i. Ohkoshi and K. NozaKI, *J. Am. Chem. Soc.*, 2012, **134**, 19989; (f) Y. J. Yu, F. L. Zhang, J. Cheng, J. H. Hao, W. T. Deng and Y. F. Wang, *Org. Lett.*, 2018, **20**, 24; (g) L. Zhang and L. Jiao, *Chem. Sci.*, 2018, DOI: 10.1039/c8sc00008e.
- 9 For selected examples on the phosphine-boryl radical, see: (a) D. H. R. Barton and M. Jacob, *Tetrahedron Lett.*, 1998, **39**, 1331; (b) A. J. Rosenthal, M. Devillard, K. Miqueu, G. Bouhadir and D. Bourissou, *Angew. Chem., Int. Ed.*, 2015, **54**, 9198.
- 10 Recent examples on radical reactions involving B₂p₂, see: (a) F. Mo, Y. Jiang, D. Qiu, Y. Zhang and J. B. Wang, *Angew. Chem., Int. Ed.*, 2010, **49**, 1846; (b) A. M. Mfuh, J. D. Doyle, B. Chhetri, H. D. Arman and O. V. Larionov, *J. Am. Chem. Soc.*, 2016, **138**, 2985; (c) W. B. Liu, X. B. Yang, Y. Gao and C. J. Li, *J. Am. Chem. Soc.*, 2017, **139**, 8621; (d) A. Fawcett, J. Pradeilles, Y. Wang, T. Mutsuga, E. L. Myers and V. K. Aggarwal, *Science*, 2017, **357**, 283; (e) L. Candish, M. Teders and F. Glorius, *J. Am. Chem. Soc.*, 2017, **139**, 7440.
- 11 G. Wang, H. Zhang, J. Zhao, W. Li, J. Cao, C. Zhu and S. Li, *Angew. Chem., Int. Ed.*, 2016, **55**, 5985.
- 12 G. Wang, J. Cao, L. Gao, W. Chen, W. Huang, X. Cheng and S. Li, *J. Am. Chem. Soc.*, 2017, **139**, 3904.
- 13 For reviews on the persistent radical, see: (a) A. Studer, *Chem.-Eur. J.*, 2001, **7**, 1159; (b) A. Studer, *Chem. Soc. Rev.*, 2004, **33**, 267; (c) H. Fischer, *Chem. Rev.*, 2001, **101**, 3581; (d) A. Studer and D. P. Curran, *Angew. Chem., Int. Ed.*, 2016, **55**, 58.
- 14 (a) L. Zhang and L. Jiao, *J. Am. Chem. Soc.*, 2017, **139**, 607; (b) W.-M. Cheng, R. Shang, B. Zhao, W.-L. Xing and Y. Fu, *Org. Lett.*, 2017, **19**, 4291.
- 15 (a) I. Beletskaya and C. Moberg, *Chem. Rev.*, 2006, **106**, 2320; (b) J. Takaya and N. Iwasawa, *ACS Catal.*, 2012, **2**, 1993; (c) R. D. Dewhurst, E. C. Neeve, H. Braunschweig and T. B. Marder, *Chem. Commun.*, 2015, **51**, 9594; (d) T. Ohmura, Y. Morimasa and M. Sugimoto, *J. Am. Chem. Soc.*, 2015, **137**, 2852; (e) E. C. Neeve, S. J. Geier, I. A. I. Mkhaliid, S. A. Westcott and T. B. Marder, *Chem. Rev.*, 2016, **116**, 9091; (f) A. B. Cuenca, R. Shishido, H. Ito and E. Fernández, *Chem. Soc. Rev.*, 2017, **46**, 415–430; (g) M. B. Ansell, O. Navarro and J. Spencer, *Coord. Chem. Rev.*, 2017, **1**, 54.



- 16 (a) Y. Zhao, N. E. Schultz and D. G. Truhlar, *J. Chem. Theory Comput.*, 2006, **2**, 364; (b) Y. Zhao and D. G. Truhlar, *J. Chem. Phys.*, 2006, **125**, 194101; (c) Y. Zhao and D. G. Truhlar, *J. Phys. Chem. A*, 2006, **110**, 13126.
- 17 D. P. Chen, G. Q. Xu, Q. H. Zhou, L. W. Chung and W. J. Tang, *J. Am. Chem. Soc.*, 2017, **139**, 9767.
- 18 This new mechanism on the formation of the pyridine-boryl radical in the 4-cyanopyridine/B₂pin₂ system is different from that reported in ref. 11.
- 19 (a) A. Vasilopoulos, S. L. Zultanski and S. S. Stahl, *J. Am. Chem. Soc.*, 2017, **139**, 7705; (b) E. Yamamoto, M. J. Hilton, M. Orlandi, V. Saini, F. D. Toste and M. S. Sigman, *J. Am. Chem. Soc.*, 2016, **138**, 15877.
- 20 X. C. Pan, E. Lacôte, J. Lalevée and D. P. Curran, *J. Am. Chem. Soc.*, 2012, **134**, 5669.
- 21 R. Shintani and K. Nozaki, *Organometallics*, 2013, **32**, 2459–2462; D. S. Laitar, E. Y. Tsui and J. P. Sadighi, *J. Am. Chem. Soc.*, 2006, **128**, 11036.

