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Iron-catalyzed boration of allylic alcohols with H_3BO_3 as an additive

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ABSTRACT

A method for the synthesis of allylboronates by iron-catalyzed boration of allylic alcohols with H_3BO_3 as an additive is developed. The introduction of H_3BO_3 promotes the cleavage of C–O bond in allylic alcohols obviously. Functional groups, such as fluoro, chloro, bromo, alkyl, and alkoxy, are tolerated well. Thus, various allylboronates are obtained in acceptable yield.

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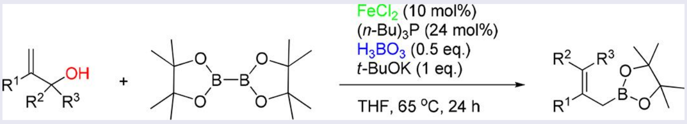
Allylboronates; allylic alcohols; boration; boric acid; iron-catalysis

GRAPHICAL ABSTRACT



Introduction

Owing to the importance in synthetic organic chemistry,[1] the synthesis of allylboronates has received much attention.[2] Compared with the transmetalation of allylic lithiums or allylic magnesiums to the boron,[3] the traditional method to obtain allylboronates, the metal catalyzed boration of allylic derivatives or 1,3-dienes has been found to be an efficient way owing to the widely functional group tolerance and mild reaction conditions. Inspired by the pioneering work of Miyaura et al. on palladium catalyzed boration of allylic esters,[4] diverse allylic boronates have been synthesized through palladium, nickel, or copper catalyzed boration of allylic halides or allylic esters.[5] Compared with allylic esters and halides, the direct use of allylic alcohols is more beneficial. One reason is that allylic esters and halides are derivatives of allylic alcohols, which is easier to obtain. The other one is that water is generated as a co-product in the reaction of allylic alcohols whereas allylic esters and halides afford corresponding salt wastes. Although Pd-catalyzed versions have been intensively studied,[6] direct boration of allylic alcohol through more economic and sustainable approaches, such as those catalyzed/promoted by base-metal salts or copper,[7] are scarce. To promote the cleavage of C-O bond in allylic alcohols, an efficient way is adding some Lewis acids,[8] such as boron reagents,[9] as additives. Recently, our group also focused on the boration of alkenes using

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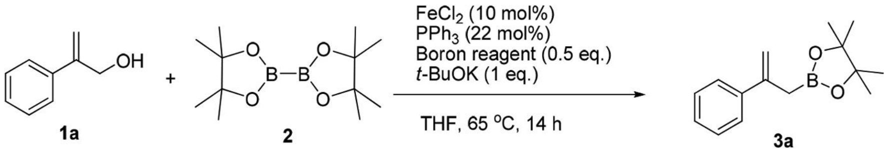
low cost, low toxicity and environmentally friendly iron catalyst.[10] As a consequence, the synthesis of allylic boronates through $FeCl_2$-catalyzed boration of allylic esters was achieved.[10c] However, the reaction of allylic alcohols gave poor yield in the previous study. In this context, we describe our further study on the iron-catalyzed direct boration of allylic alcohols with H_3BO_3 as an additive to promote the cleavage of C-O bond.

Results and discussion

The iron-catalyzed direct boration of allylic alcohols was initiated with 2-phenylprop-2-en-1-ol (**1a**) as a model substrate. At the outset, several boron reagents were investigated as additives to promote the cleavage of C-O bond (Table 1). Under the already established conditions for the boration of allylic esters,[10c] the reaction of allylic alcohols gave poor yield (Table 1, entry 1). To our delight, the introduction of $PhB(OH)_2$ improved the yield obviously (Table 1, entry 2). The highest yield was achieved when 0.5 eq. of H_3BO_3 was used while $B(OMe)_3$ had almost no effect on the reaction (Table 1, entries 3 and 4). Both increasing and decreasing the amount of H_3BO_3 resulted in the decrease of the yield (Table 1, entries 5 and 6). Analysis of the crude product by ^1H NMR showed that **1a** was totally consumed and some new materials with similar signals with **1a** were formed besides **3a**. We speculated they were adducts of **1a** and the boron species. That is why high conversion of **1a** was determined in all cases.

It is well known that the ligands may adjust the electronic and steric character of the metal center, thus affecting the activity and selectivity of the catalyst. So the effect of the ligands was explored (Table 2). Without additional ligand, the reaction can also proceed but with a lower yield (Table 2, entry 1). In the screened phosphine and nitrogen ligands (Table 2, entries 2–10), $(n\text{-Bu})_3P$ gave the highest yield (Table 2, entry 5). Upon slightly increasing the ligand loading to 24 mol%, a higher yield of 68% was achieved (Table 2, entry 11). But the yield was not increased anymore when the ligand loading was further increased to 30 mol% (Table 2, entry 12). In addition, similar to our previous reports on the iron catalyzed boration of alkenes,[10] no desired product was detected in the absence of a base (Table 2, entry 13).

Table 1. Optimization of boron reagents.[a]



Entry	Boron reagent	Yield[b] (%)
1	–	16
2	$PhB(OH)_2$	57
3	H_3BO_3	62
4	$B(OMe)_3$	17
5[c]	H_3BO_3	37
6[d]	H_3BO_3	32

[a] Reaction conditions: **1a** (0.3 mmol), **2** (0.45 mmol), $FeCl_2$ (0.03 mmol), PPh_3 (0.066 mmol), t-BuOK (0.3 mmol), boron reagent (0.5 eq.) in THF (2 mL) at 65 °C for 14 h.
[b] Yield was determined by ^1H NMR with 1,1,2,2-tetrachloroethane as an internal standard.
[c] H_3BO_3 (0.09 mmol, 0.3 eq.).
[d] H_3BO_3 (0.3 mmol, 1 eq.).
THF, tetrahydrofuran.

Table 2. Optimization of ligands.[a]

Entry	Ligand	Yield[b](%)
1	–	51
2	Ph_3P (20 mol%)	56
3	Xantphos (10 mol%)	35
4	DPPF (10 mol%)	55
5	$(n\text{-Bu})_3P$ (20 mol%)	66
6	$(t\text{-Bu})_3P$ (20 mol%)	59
7	Tricyclohexylphosphine (20 mol%)	54
8	X-phos (20 mol%)	20
9	1,10-Phenanthroline (10 mol%)	55
10	TMEDA (10 mol%)	44
11	$(n\text{-Bu})_3P$ (24 mol%)	68
12	$(n\text{-Bu})_3P$ (30 mol%)	67
13[c]	$(n\text{-Bu})_3P$ (24 mol%)	0

[a] Reaction conditions: **1a** (0.6 mmol), **2** (0.9 mmol), $FeCl_2$ (0.06 mmol), ligand, *t*-BuOK (0.6 mmol), H_3BO_3 (0.3 mmol) in THF (2 mL) at 65 °C for 24 h.
[b] Yield was determined by ^1H NMR with 1,1,2,2-tetrachloroethane as an internal standard.
[c] Without *t*-BuOK.
Xantphos, 4,5-bis(diphenylphosphino)-9,9-dimethylxanthene; X-phos, 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl. DPPF, 1,1′-bis(diphenylphosphino)ferrocene; TMEDA, tetramethylethylenediamine.

The catalytic performance of other transition metal salts were also examined (Table 3). Compared with $FeCl_2$, other metal chlorides, such as CuCl, $PdCl_2$, and $NiCl_2$, exhibited lower activity (Table 3, entries 1–3). The use of high-purity (99.99%) $FeCl_2$ as the catalyst gave a higher yield of 70% (Table 3, entry 5), while no desired product was obtained without $FeCl_2$ (Table 3, entry 6). The above results suggest that the reaction is catalyzed by iron.

In addition, the influence of solvent was explored (Table 4). In general, ethers gave better results (Table 4, entries 1–4), and tetrahydrofuran (THF) was the best one (Table 4, entry 1). A lower yield was obtained when DMF was used (Table 4, entry 5).

Table 3. Optimization of transition metal catalysts.[a]

Entry	Catalysis	Yield[b] (%)
1	CuCl	29
2	$PdCl_2$	13
3	$NiCl_2$	53
4	$FeCl_2$	68
5[c]	$FeCl_2$	70
6	–	0

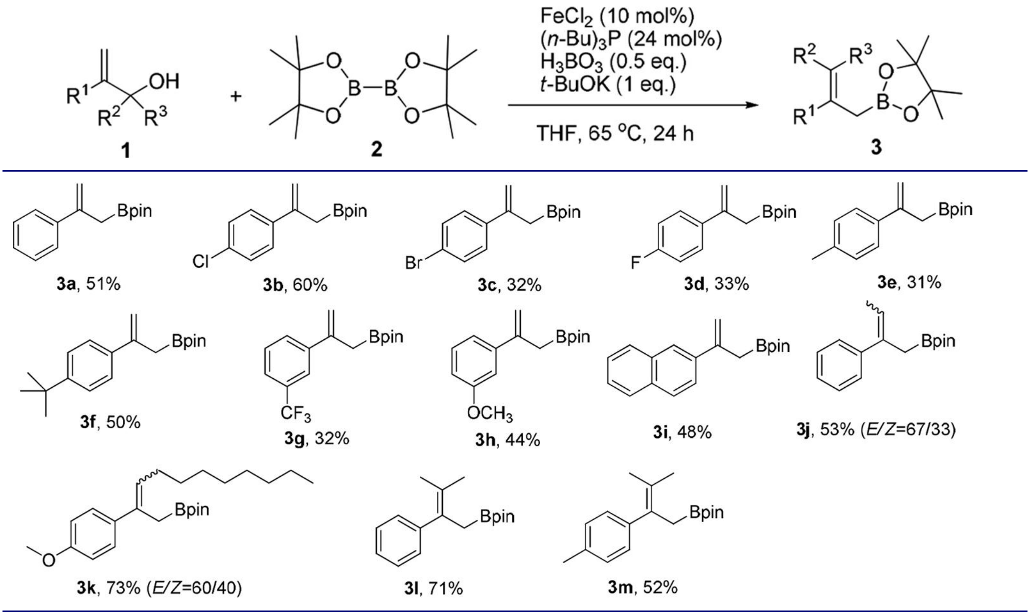
[a] Reaction conditions: **1a** (0.6 mmol), **2** (0.9 mmol), catalysis (0.06 mmol), $(n\text{-Bu})_3P$ (0.144 mmol), *t*-BuOK (0.6 mmol), H_3BO_3 (0.3 mmol) in THF (2 mL) at 65 °C for 24 h.
[b] Yield was determined by ^1H NMR with 1,1,2,2-tetrachloroethane as an internal standard.
[c] $FeCl_2$ (99.99%, 10 mol%).
THF, tetrahydrofuran.

Table 4. Optimization of reaction solvents.[a]

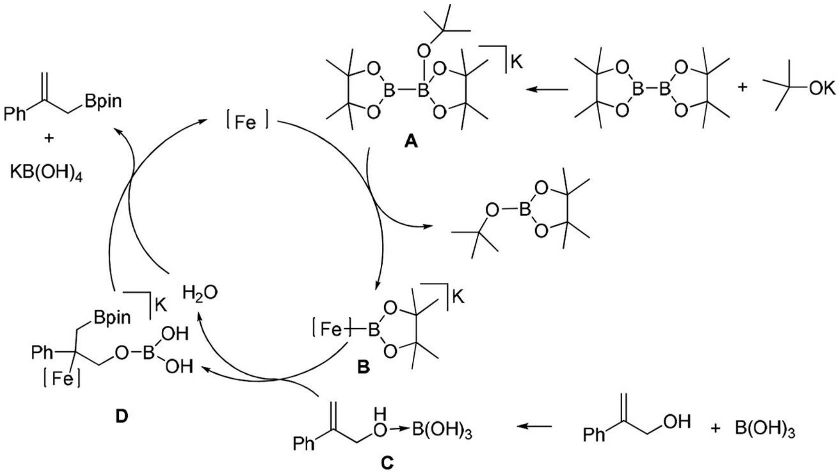
Entry	Solvent	Yield[b] (%)
1	THF	68
2	*t*-BuOMe	60
3	dioxane	48
4	1,2-Dimethoxyethane	62
5	DMF	37

[a] Reaction conditions: **1a** (0.6 mmol), **2** (0.9 mmol), $FeCl_2$ (0.06 mmol), $(n\text{-Bu})_3P$ (0.144 mmol), *t*-BuOK (0.6 mmol), H_3BO_3 (0.3 mmol) in solvent (2 mL) at 65 °C for 24 h.
[b] Yield was determined by ^1H NMR with 1,1,2,2-tetrachloroethane as an internal standard.
DMF, dimethylformamide; THF, tetrahydrofuran.

Table 5. Reaction of variously substituted allylic alcohols with B_2pin_2.



Having established the optimized reaction conditions, the scope in terms of allylic alcohols was explored (Table 5). Various allylic alcohols bearing either electron-withdrawing or electron-donating groups were converted smoothly into the corresponding allylboronates in acceptable yield. Functional groups, such as chloro, fluoro, bromo, alkyl, and alkoxy, were tolerated well. 2-(Naphthalen-2-yl)prop-2-en-1-ol afforded the corresponding product in 48% yield. α-Substituted allylic alcohols were also converted into the desired products in moderate to good yields. It is worth pointing out that a mixture of *E*/*Z* configuration products was obtained for α-mono-substituted substrates.



Scheme 1. Proposed mechanism for iron-catalyzed boration of allylic alcohol.

On the basis of the previous study on the mechanism of boration,[11] addition/elimination of allylic carbonates[5a,b] and activation of hydroxy group by boron reagents,[6e,9a,b] a possible reaction mechanism using **1a** as a representative substrate was shown in Scheme 1. The complex **A**, formed through addition of *t*-BuOK to B_2pin_2, was suffered a B-B bond cleavage with the release of *t*-BuOBpin to generate the FeB intermediate (**B**). Meanwhile, **1a** was coordinated to H_3BO_3 to form a complex **C**, which was further coordinated to the intermediate **B** followed by the insertion of C=C double bond to the Fe–B bond to generate intermediate **D**. Finally, the product was obtained after the release of $KB(OH)_4$ with regeneration of the active Fe catalyst. Although a boronate *t*-BuOBpin was generated, it was not an efficient activator for hydroxyl group in this reaction. That agrees with the low activity of $B(OMe)_3$ (Table 1, entry 4).

Conclusion

In summary, the first iron-catalyzed boration of allylic alcohols with H_3BO_3 as an additive has been described. Various allylic alcohols bearing either electron-withdrawing or electron-donating groups, such as fluoro, chloro, bromo, alkyl, and alkoxy, were converted smoothly into corresponding allylboronates in acceptable yield. This method was also suitable for α -substituted allylic alcohols, and a mixture of *E*/*Z* configuration products was obtained for α -mono-substituted substrates.

Experimental

^1H NMR (400 MHz) were recorded on a Bruker AVANCE II-400 spectrometer with chemical shifts reported as ppm (in $CDCl_3$, with TMS as an internal standard). ^{13}C NMR (101 MHz) were recorded on a Bruker AVANCEII-400 spectrometer with chemical shifts reported as ppm (in $CDCl_3$, with $CDCl_3$ as an internal standard). High resolution mass spectra (ESI) were recorded on a Micromass Waters Q-TOF Microspectrometer. Unless otherwise noted, all reactions were performed under argon using Schlenk line techniques or in a glovebox with magnetic stirring. Solvents were dried by passage through an activated alumina column under argon. Column chromatography was performed on silica gel (200–300 mesh). High-purity $FeCl_2$ (beads, 99.99%, Sigma-Aldrich) powder was prepared using a mortar and pestle in a glovebox. Other reagents and the substrates were purchased and used as received.

General procedure for the synthesis of allylboronates (3)

To a Schlenk tube equipped with a magnetic stir bar and charged with $FeCl_2$ (13 mg, 0.1 mmol) was added THF (6 mL), followed by aryl allylic alcohols (1.0 mmol), H_3BO_3 (30.9 mg, 0.5 mmol), bis(pinacolato)diboron (381 mg, 1.5 mmol), *t*-BuOK (113 mg, 1.0 mmol) and $P(Bu\text{-}n)_3$ (48.6 mg, 0.24 mmol). The resulting mixture was stirred at 65 °C for 24 h. Then, brine (20 mL) was added and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed in vacuum. The resultant crude product material was purified by flash chromatography using the appropriate gradient of petroleum ether and EtOAc.

2-(2-Phenylallyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3a)[10c]

Colorless liquid, yield 51%; ^1H NMR (400 MHz, $CDCl_3$, Me_4Si) δ 7.52–7.50 (m, 2H), 7.30–7.26 (m, 2H), 7.35–7.31 (m, 1H), 5.40 (d, $J = 1.3$ Hz, 1H), 5.14 (d, $J = 1.3$ Hz, 1H), 2.21

(s, 2H), 1.20 (s, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.4, 141.9, 128.1, 127.2, 125.9, 112.2, 83.4, 24.6.

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