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Boron-catalysed transition-metal-free arylation and alkenylation of allylic alcohols with boronic acids†

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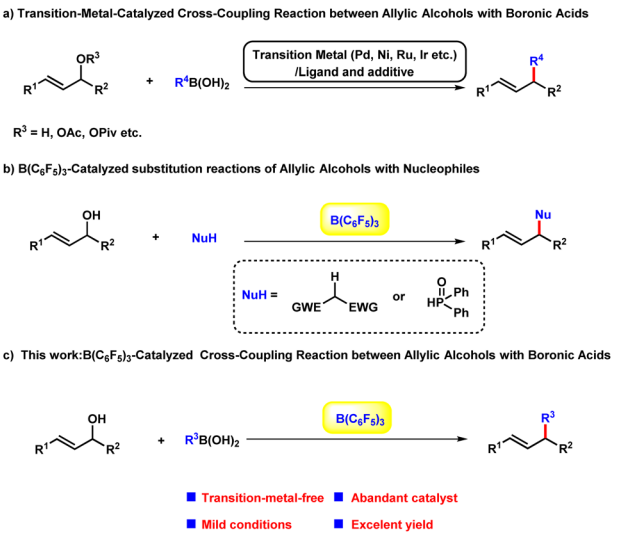
The development of efficient catalytic reactions with excellent atom and step economy employing sustainable catalysts is highly sought-after in chemical synthesis to reduce the negative effects on the environment. The most commonly-used strategy to construct allylic compounds relies on the transition-metal-catalysed nucleophilic substitution reaction of allylic alcohol derivatives. These syntheses exhibit good yield and selectivity, albeit at the expense of toxic and expensive catalysts and extra steps. In this paper, we report a transition-metal-free arylation and alkenylation reaction between unprotected allylic alcohols and boronic acids. The reactions were performed with $B(C_6F_5)_3$ as the catalyst in toluene, and corresponding products were obtained in 23–92% yields. The reaction has mild conditions, scalability, excellent atom and step economy.

Allylic alkylation and alkenylation of allylic reagents such as allylic halides, carboxylates, carbonates, phosphates, and related compounds are some of the most important textbook reactions for carbon–carbon bond-forming, and have been widely applied in the syntheses of a broad scope of complex molecules.[1] Among these dozens of building blocks, the direct transformation of allylic alcohols would be highly beneficial from the viewpoint of sustainable chemistry:[1h,2] (a) the substrate could be used without the pre-activation of the hydroxyl group; (b) avoidance of other undesired by-products other than water. Regarding the other reaction partner, boronic acids[3] are a promising choice compared with halides, grignard reagents and other feedstocks due to their stability, operational convenience, negligible toxicity, and broad functional group compatibility. A number of transition-metal-catalysed cross-coupling reactions between allylic alcohols and boronic acids have been established based on π-allyl metal complexes with outstanding efficacy and selectivity in a long-range.[4] However, these cases bear the intrinsic limitations of the transition-metal-catalysts, which are widely regarded as expensive, hard to prepare, oxygen and moisture sensitive. As an alternative, several Brønsted and Lewis acids catalysed substitution reaction of allylic alcohols with different nucleophiles have been explored as the environmental benign approaches to obtain allylic compounds.[5] In 2015, Gandon[6] group reported a alkenylation of alcohols with vinylboronic acids employing air stable calcium(II) complex as the catalyst. Despite of these progresses, the green and sustainable catalytic arylation protocol between alcohols and boronic acids remain underdeveloped. In the last decade, $B(C_6F_5)_3$ has been realized to be capable of initiating a wide range of chemical transformations with remarkable performance.[7] In particular, the cross-coupling reaction of alcohols to form C–C and C–P bond have been achieved with



Scheme 1 Catalytic cross-coupling reaction between boronic acids and allylic alcohol derivatives.

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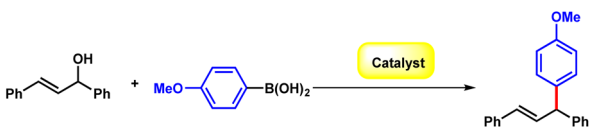
$B(C_6F_5)_3$ by Xie[8] *et al.* very recently. Herein, as our longstanding interest in the development of environmental-friendly chemical transformations, we envisaged to explore the efficacy of $B(C_6F_5)_3$ in the arylation and alkenylation reaction of allylic alcohols (Scheme 1).

Initially, the (*E*)-1,3-diphenylprop-2-en-1-ol **1a** and 4-methoxyphenylboronic acid **2a** were chosen as the model substrates to optimize the reaction conditions. The reaction of **1a** and **2a** was carried out in the presence of $B(C_6F_5)_3$ (20 mol%) at 80 °C in MeCN, affording compound **3a** in 57% yield (Table 1, entry 1). Delighted by this initial result, we investigated the reaction conditions comprehensively. The screening of the solvent indicated that the yield could be promoted to 71% in nonpolar methylbenzene (Table 1, entry 2–7). Lewis acid catalysts such as $Cu(OTf)_2$, $Zn(OTf)_2$, and $Sc(OTf)_2$ were evaluated to offer the desired product only in moderate yield (Table 1, entries 8–10). Moreover, other boron containing catalysts including $B(OH)_3$ and $BF_3{\cdot}OEt_2$ only offered diminished yields as low as 32% (Table 1, entries 11–12). In consideration of that the unstability of alcohols in presence of the strong Lewis acid catalyst, we increased **1a** to 1.2 equivalent and more, up to 96% yield was obtained with 2.0 equivalent of **1a** (Table 1, entries 13–15). The desired product could also be obtained in 93% yield with a reduced amount of $B(C_6F_5)_3$ of 10% (Table 1, entries 16–17). Then, we conducted the reaction at lower temperature, and the results indicated that the reaction performed smoothly at ambient temperature giving 91% yield (Table 1, entries 18–19).

With improved reaction conditions in hand, the scope of the boron-catalysed cross coupling reaction was explored between a set of di-aryl allylic alcohols and boronic acids. At first, the substituent effects on the benzene ring of **1** was evaluated. Delightfully, both electric-donating and -withdrawing groups were well tolerated with the conditions. When methyl substituted allylic alcohol on the para-position was tested, 58% yield was obtained (**3b**). Products with halogen groups such as fluorine, chlorine and bromine were also generated in the yields up to 90% (**3c–3e**). Methyl, methoxyl and chlorine groups on meta and ortho positions of the benzene ring were also appropriate under standard conditions offering **3f** to **3i** in the yields of 23–78%. When the benzene ring was replaced with 2-naphthalene, the corresponding product was prepared in 45% yield (**3j**). Next, the scope of boronic acids were also explored. Apart from **2a**, phenylboronic acid bearing a series of electron-rich groups such as alkoxyl, methylthio and dimethylamino groups were compatible with this protocol affording corresponding products **3k–3o** in the yields of 45–90%. Further evaluation employing alkyl substituent allylic alcohol such as (*E*)pent-3-en-2-ol failed to yield the desired product. Later, several aryboronic acids including (4-methoxynaphthalen-1-yl) boronic acid, indole-5-

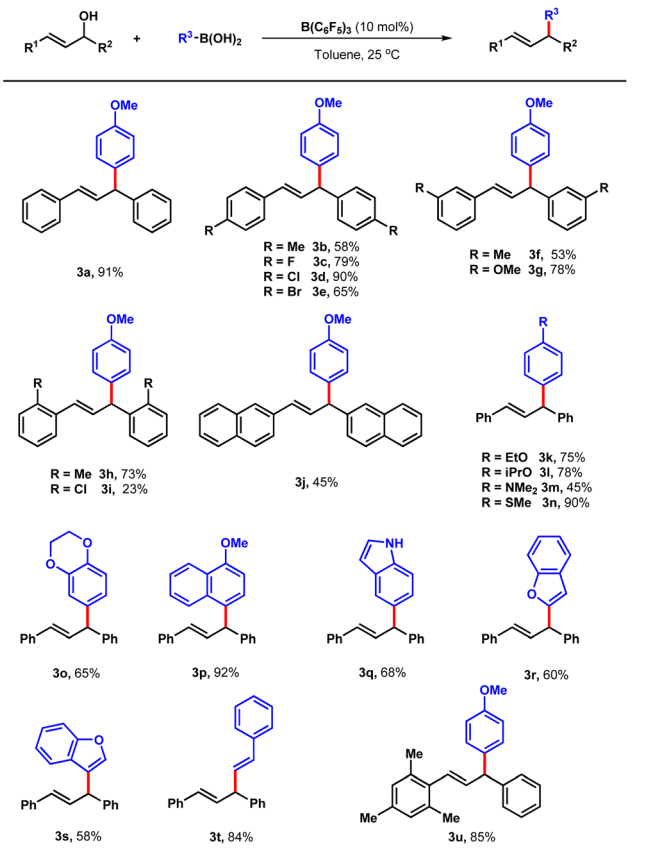
Table 1 The optimization of the conditions[a]



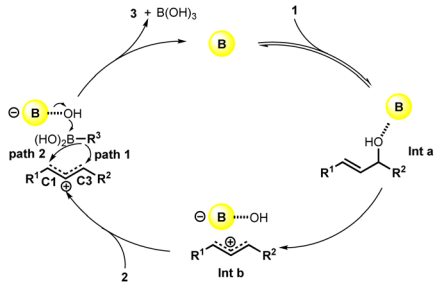
Entry	Catalyst	Solvent	Temperature (°C)	Yield[b]
1	$B(C_6F_5)_3$	CH_3CN	80	57%
2	$B(C_6F_5)_3$	DMF	80	38%
3	$B(C_6F_5)_3$	DMSO	80	25%
4	$B(C_6F_5)_3$	THF	80	18%
5	$B(C_6F_5)_3$	DCE	80	62%
6	$B(C_6F_5)_3$	EA	80	12%
7	$B(C_6F_5)_3$	Toluene	80	71%
8	$Cu(OTf)_2$	Toluene	80	55%
9	$Zn(OTf)_2$	Toluene	80	52%
10	$Sc(OTf)_2$	Toluene	80	63%
11	$B(OH)_3$	Toluene	80	36%
12	$BF_3{\cdot}OEt_2$	Toluene	80	32%
13[c]	$B(C_6F_5)_3$	Toluene	80	88%
14[d]	$B(C_6F_5)_3$	Toluene	80	91%
15[e]	$B(C_6F_5)_3$	Toluene	80	96%
16[f]	$B(C_6F_5)_3$	Toluene	80	93%
17[g]	$B(C_6F_5)_3$	Toluene	80	85%
18	$B(C_6F_5)_3$	Toluene	50	90%
19[h]	$B(C_6F_5)_3$	Toluene	25	91%

[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), catalyst (20 mol%), solvent (2 mL), 6 hours, under air atmosphere. [b] Isolated yield. [c] 1.2 equiv. of **1a** was added. [d] 1.5 equiv. of **1a** was added. [e] 2.0 equiv. of **1a** was added. [f] 10 mol% of $B(C_6F_5)_3$ was used. [g] 5 mol% of $B(C_6F_5)_3$ was used. [h] The reaction time is 36 hours.

Table 2 Scope of the reaction[a]



[a] Reaction conditions: **1** (0.1 mmol), **2** (0.2 mmol), $B(C_6F_5)_3$ (10 mol%), toluene (2 mL), 36 hours, under air atmosphere.



Scheme 2 Proposed reaction pathway.

boronic acid, benzofuran-3-boronic acid and benzofuran-2-boronic acid provided the desired products **3p–3s** in 58–92% yields. Moreover, alkenyl boric acid was also evaluated offering **3t** in the yield of 84%. It is always challenging to control the regio-selectivity of the nucleophilic substitution for unsymmetrical allylic alcohols.[9] When electron deficient boronic acids such as (perfluorophenyl)boronic acid and pyridine heterocycle boronic acid were tested under the optimized conditions, the reaction did not occur with the boronic acids recovered. The regio-selectivity of this kind of reaction is later, to illustrate the regio-selectivity of the protocol further, the unsymmetrical allylic alcohol **1u** was loaded to the standard conditions, and **3u** was obtained as the only products in 85% yield, which emphasize the excellent selectivity of the reaction (Table 2).

Based on previous reports,[8] the reaction mechanism was proposed as shown in Scheme 2. At first, the coordination of the $B(C_6F_5)_3$ catalyst with the alcohol generated the intermediate a (**Int a**), which tend to offer the carbocation intermediate b (**Int b**) after the cleavage of C–O bond. Later, the migration of R^3 to C1 or C3 position occurred to generate the desired product 3 and boric acid with the $B(C_6F_5)_3$ catalyst recovered. The selectivity between the C1 or C3 arylation mainly depends on the steric effect of R^1 and R^2.

Conclusions

In conclusion, we have established an efficient and convenient cross-coupling reaction between allylic alcohols and boronic acids under transition-metal-free conditions. This boronic-catalysed protocol exhibited excellent selectivity, mild conditions and broad scope.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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