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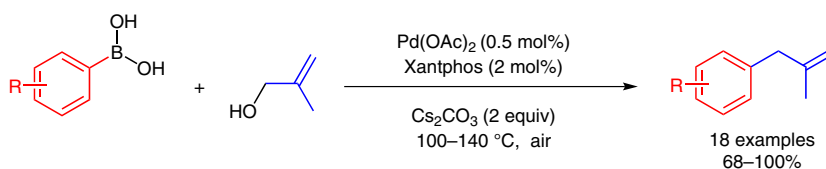
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An Efficient Method for the Synthesis of 2-Methylallyl Alkenes by Cross-Coupling Reactions

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Abstract To obtain aromatic 2-methylallyl derivatives, cross-coupling reactions between 2-methyl-2-propen-1-ol and various boronic acids were studied. Among allylic alcohols described for such cross-coupling reactions, 2-methyl-2-propen-1-ol has a low reactivity. Indeed, this substrate did not react with several boronic acids under the previously described conditions and new reaction conditions were investigated. We describe herein a new protocol with small amounts of palladium and ligand, without any additive solvent and under microwave heating. A subsequent simple distillation process not only leads to the product, but also allows the 'reagent-solvent' to be recycled for further cross-coupling reactions, without loss of yield. Scope and limitations were studied. Furthermore, when this easy cross-coupling reaction was extended to a wide range of organoboronic acids, high functional group tolerance was observed and a new series of alkenes was synthesized in good yields.

Key words palladium, cross-coupling reactions, methylallyl alkenes, boronic acids, allyl alcohols

Leishmaniasis is an infectious disease caused by *Leishmania donovani*: there are more than 50000 deaths a year due to the visceral form (VL).¹ However, most drugs have either too great parasitic resistance (pentamidine) or too high cost (liposomal amphotericin B).² Thus, there is a real need for new drugs that are resistance-free and less expensive, and can be administered orally.

Focusing on amidoxime substrates, our group has previously described the preparation of monoamidoxime derivatives: an oxidative free-radical mechanism mediated by manganese(III) acetate allowed the cyclization of alkenes with β -keto sulfones³ bearing a nitrile group to give amidoxime derivatives. The biological assessment of this series highlighted a hit [selectivity index (SI) = 6.37; Figure 1],⁴ and further pharmacomodulations of the amidoxime deriv-

atives showed that the R¹ aromatic moiety must be linked to the dihydrofuran by a methylene group to retain the antileishmanial activity (Scheme 1).⁵

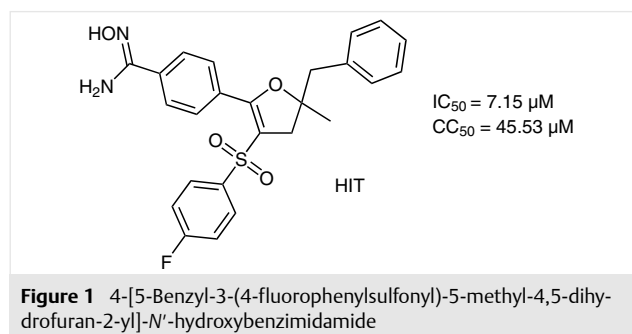
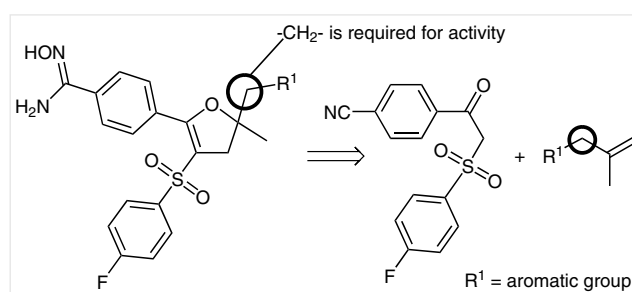


Figure 1 4-[5-Benzyl-3-(4-fluorophenylsulfonyl)-5-methyl-4,5-dihydrofuran-2-yl]-N'-hydroxybenzimidamide

In connection with our program centered on the preparation of new, potentially bioactive compounds,⁶ aiming at exploring deeper SARs of the amidoxime series, we needed to synthesize new compounds using various 2-methylallyl derivatives. However, few aromatic 2-methylallyl derivatives are commercially available and very few publications have addressed the synthesis of these particular alkenes.⁷

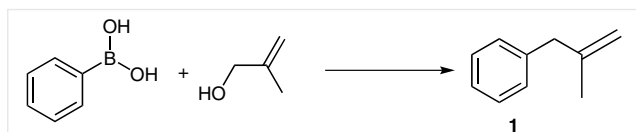


Scheme 1 Alkene structure required for the synthesis of new amidoxime derivatives

The use of methallyl alcohol (2-methyl-2-propen-1-ol) in cross-coupling reactions is a real challenge, since it is known to be a poor reactive substrate as hydroxy is a poor leaving group.^{7h} In light of the above, we decided to synthesize a new series of alkenes by employing cross-coupling reactions between 2-methyl-2-propen-1-ol and various organoboronic acids. Cross-coupling reactions between allyl alcohols and organoboronic acids have already been described;^{7f-h,8} unfortunately, starting from the previous protocols, using no base^{7f-h} or catalytic amounts of base in water,⁸ we did not obtain the required cross-coupled products. For example, *o*-methylphenylboronic acid or *p*-nitrophenylboronic acid did not react with methallyl alcohol in the presence of Pd₂(dba)₃·CHCl₃/(PhO)₃P in toluene at 100 °C.^{7g} Similarly, *o*-methylphenylboronic acid or *p*-cyanophenylboronic acid did not react with methallyl alcohol in the presence of Pd(Ph₃)₄ in refluxing dioxane or tetrahydrofuran.^{7f,h} We hypothesized that the lower cross-coupling reactivity of methallyl alcohol relative to other allyl alcohols and/or the versatility of the substituted boronic acid reactivity are involved.^{7f}

A new protocol has now been established, allowing the use of a wider range of organoboronic acids. Our prior experience with palladium-catalyzed cross-coupling reactions has facilitated the synthesis of new alkenes.⁹

Phenylboronic acid was initially chosen as it is the simplest arylboronic acid, without any substituent that could influence reactivity (Scheme 2). Previous studies on allylic alcohol cross-coupling reactivity have investigated various organic solvents such as toluene, dioxane or dichloromethane. In an elegant study, Manabe and co-workers⁸ have also described the first cross-coupling reaction of an allylic alcohol in water. Following their lead, we decided to use water or another environmentally benign solvent.



Scheme 2 Synthesis of (2-methylallyl)benzene (1)

Our preliminary investigations had shown that 2-methyl-2-propen-1-ol did not react with substituted boronic acids under classical conditions without the presence of a base. Therefore, the influence of temperature and base needed to be assessed first (Table 1).

Assays pointed to a need for heating to carry out the cross-coupling reaction (Table 1, entries 1–4). The outcomes highlighted the need for a strong base for an optimal cross-coupling reaction: the yield was increased twofold by replacing potassium carbonate with cesium carbonate (Table 1, entries 4 and 9).¹⁰ Although the exact role of the base remains unclear, yields of cross-coupling reactions of allylic

Table 1 Assessment of the Influence of Temperature and Base^a

Entry	Base	Temp (°C)	Time (h)	Yield (%) of 1
1	none	r.t.	12	0
2	K ₂ CO ₃ (2 equiv)	r.t.	3	0
3	K ₂ CO ₃ (2 equiv)	140	1.5	2
4	K ₂ CO ₃ (2 equiv)	140 ^b	1	11
5	NaOH (0.05 equiv)	140 ^b	1.5	0
6	NaOH (1 equiv)	140 ^b	1.5	5
7	NaOH (2 equiv)	140 ^b	1.5	11
8	<i>t</i> -BuOK (2 equiv)	140 ^b	1	7
9	Cs ₂ CO ₃ (2 equiv)	140 ^b	1	22

^a Typical reaction conditions: H₂O as solvent, N₂ atmosphere, Pd(PPh₃)₄ (5 mol%) as the catalyst system.

^b Reaction implemented under microwave irradiation in a sealed reactor.

alcohols in water are supposed to be increased with a catalytic amount of base.⁸ Herein, stoichiometric amounts of a strong base were needed, probably because of the low reactivity of methallyl alcohol. Subsequent cross-coupling reactions were conducted with 2 equivalents of cesium carbonate at 140 °C under microwave irradiation for one hour. The catalyst system conditions were then assessed by using various phosphine types of ligand (Table 2).

Table 2 Assessment of the Influence of the Catalyst System^a

Entry	Catalyst	Additional ligand	Yield (%) of 1
1	–	–	0
2	Pd ₂ (dba) ₃	–	2
3	Pd ₂ (dba) ₃	Ph ₃ P	18
4	Pd ₂ (dba) ₃	BINAP	24
5	Pd(OAc) ₂	–	7
6	Pd(OAc) ₂	Ph ₃ P	9
7	Pd(OAc) ₂	BINAP	11
8	Pd(dppf)Cl ₂	–	13
9	Pd(PPh ₃) ₂ Cl ₂	–	22
10	Pd(dppf)Cl ₂	Ph ₃ P	9
11	Pd(OAc) ₂	Xantphos	29

^a Typical reaction conditions: H₂O as solvent, N₂ atmosphere, Cs₂CO₃ as base, catalyst (5 mol%), additional ligand (10 mol%) if applicable, heating at 140 °C under microwave irradiation for 1 h in a sealed reactor.

There was no cross-coupling reaction without a catalyst (Table 2, entry 1), which excludes an addition/elimination pathway.¹¹ Reactions were more efficient when palladium(II) combined with a ligand was used, and bidentate ligands showed a better catalytic activity (Table 2, entries 2–11). Bidentate ligands such as Xantphos, usually used for palladium-catalyzed carbon–nitrogen¹² bond-forming reactions, have also previously proven to be effective in carbon–

carbon bond formation. Thus, subsequent cross-coupling reactions were conducted with palladium(II) acetate as catalyst and Xantphos as ligand. Atmospheric conditions and solvents were then assessed (Table 3).

Table 3 Assessment of the Influence of Solvent^a

Entry	Solvent	Atmosphere	Yield (%) of 1
1	H ₂ O	air	55
2	PEG 400	air	33
3	2-methyl-2-propen-1-ol	air	66

^a Typical reaction conditions: Cs₂CO₃ as base, Pd(OAc)₂ (5 mol%) as catalyst, Xantphos (10 mol%) as ligand, heating at 140 °C under microwave irradiation for 1 h in a sealed reactor.

Cross-coupling reactions are usually carried out under inert atmosphere because palladium catalysts could be air-sensitive.^{7b,c} Surprisingly, yields were higher for reactions under air atmosphere (Table 3, entry 1) than under nitrogen atmosphere (Table 2, entry 11), which suggests that oxygen in the air could enhance reactivity.

Using methallyl alcohol without any additive solvent provided the best yield (Table 3, entry 3), and a two-step distillation process under reduced pressure allowed the product to be quickly obtained in good yield. First, 2-methyl-2-propen-1-ol is withdrawn at 80 °C/600 torr and then the cross-coupled product is obtained at 180 °C/600 torr. It should be emphasized that distilled solvent (2-methyl-2-propen-1-ol) can be recycled for at least three cross-coupling assays without any loss of reactivity. Subsequent cross-coupling reactions were therefore carried out under air conditions and with no additive solvent, using 2-methyl-2-propen-1-ol as both reagent and solvent.

As it has been clearly established that the amount of catalyst/ligand significantly affects yields, several assays were carried out to determine the best catalyst/ligand ratio (Table 4).^{7h,13}

Table 4 Assessment of the Influence of the Catalyst/Ligand Ratio^a

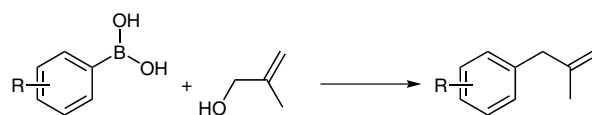
Entry	Pd(OAc) ₂ (mol%)	Xantphos (mol%)	Yield (%) of 1
1	1	2	65
2	0.5	1	65
3	0.5	2	88
4	0.05	0.2	66

^a Typical reaction conditions: no additive solvent, air atmosphere, Cs₂CO₃ as base, Pd(OAc)₂ as catalyst, Xantphos as ligand, heating at 140 °C under microwave irradiation for 1 h in a sealed reactor.

The most efficient ratio found was ligand/catalyst 4:1, which provided a greatly improved yield (Table 4, entry 3). Hence, subsequent cross-coupling reactions were carried out using this ligand/catalyst ratio.

The range of the reaction was explored using various organoboronic acids under the optimal reaction conditions previously established (Table 5); as before, purification of the cross-coupled products was carried out by distillation.

Table 5 Cross-Coupled Products from the Reaction of 2-Methyl-2-propen-1-ol with Organoboronic Acids



Entry	R	Product	Yield (%)
1	<i>o</i> -Me	2	86 ^a
2	<i>m</i> -Me	3	74 ^b
3	<i>p</i> -Me	4	100 ^a
4	<i>o</i> -Br	5	81 ^b
5	<i>p</i> -Br	6	92 ^a
6	<i>o</i> -NO ₂	7	92 ^c
7	<i>m</i> -NO ₂	8	76 ^a
8	<i>p</i> -NO ₂	9	70 ^a
9	<i>p</i> -Ph	10	94 ^a
10	<i>o</i> -CN	11	68 ^c
11	<i>m</i> -CN	12	85 ^a
12	<i>p</i> -CN	13	95 ^a
13	<i>p</i> -CH=CH ₂	14	77 ^a
14	<i>p</i> -B(OH) ₂ ^d	15	77 ^a
15	<i>o</i> -CH ₂ OH	16	0 ^{a,c}
16	<i>m</i> -CH ₂ OH	17	0 ^{a,c}
17	<i>p</i> -CH ₂ OH	18	14 ^a

^a Reaction conditions (a): Cs₂CO₃ (2 equiv), Pd(OAc)₂ (0.5 mol%), Xantphos (2 mol%), sealed reactor, air, MW, 140 °C, 1.5 h.

^b Reaction conditions (b): Cs₂CO₃ (2 equiv), Pd(OAc)₂ (0.5 mol%), Xantphos (2 mol%), sealed reactor, air, MW, 120 °C, 1 h.

^c Reaction conditions (c): Cs₂CO₃ (2 equiv), Pd(OAc)₂ (0.5 mol%), Xantphos (2 mol%), air, 100 °C, 12 h.

^d In the product **15**, R = *p*-(2-methylallyl).

Yields obtained were quite good to excellent for most products, which makes this process an easy way to provide various alkenes via an efficient palladium-catalyzed cross-coupling reaction. It is worth noting that a similar reactivity was observed for boronic acids substituted with an electron-withdrawing or an electron-donating group.

The outcomes were also indicative of the influence of the substituent position on the reactivity of the boronic acid. Comparing the same moiety, the *p*-substituted phenylboronic acid showed better reactivity than the respective *m*- and *o*-substituted phenylboronic acids. We observed deboronation side reactions for most of the *o*-substituted boronic acids when the cross-coupling reactions were performed at 140 °C, but these side reactions could be avoided by using milder reaction conditions. Therefore, when mod-

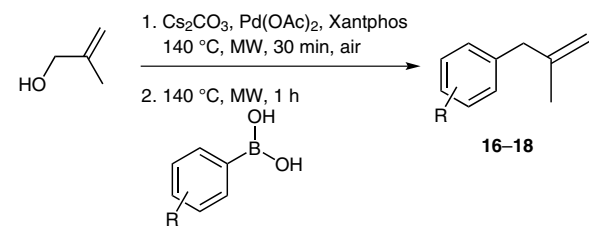
erate yields were obtained, the reaction conditions were slightly modified (mainly via lower temperature) in order to obtain yields of at least 70%.

The assay carried out with a diboronic acid afforded the decoupled product **15** in very good yield (77%; Table 5, entry 14), which suggests the high reactivity of this substrate, as the two boronic moieties reacted with the same amount of catalyst and base as used for the examples with only one boronic moiety.

Surprisingly, a very low yield was observed for product **18** (Table 5, entry 17). We hypothesize that the hydroxymethyl group of the boronic acid likely interferes with palladium (oxidative addition to palladium) and cesium carbonate (organic salt formation), which results in a strongly decreased yield of the desired cross-coupled product.

Since we observed such low yields for compounds **16–18** (Table 5, entries 15–17), we implemented a new assay: a solution of cesium carbonate, palladium(II) acetate and Xantphos in 2-methyl-2-propen-1-ol was first allowed to react, then the (hydroxymethyl)phenylboronic acid was added; the yields of alkenes obtained are listed in Table 6.

Table 6 Cross-Coupling Reactions with (Hydroxymethyl)phenylboronic Acids Using Conditions (d)



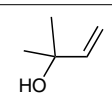
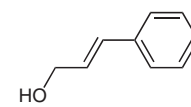
Entry	R	Product	Yield (%)
1	<i>o</i> -CH ₂ OH	16	84
2	<i>m</i> -CH ₂ OH	17	83
3	<i>p</i> -CH ₂ OH	18	90

These very good yields confirm the previous hypothesis: cesium carbonate and palladium(II) acetate interact with the hydroxymethyl group of the boronic acid. Thus, a simple modification of the order of addition of the reagents led to the expected hydroxymethyl-containing products, with a greatly enhanced reactivity. It is worth noting that there is a hindrance effect, as a better yield was obtained with the *p*-hydroxymethyl substituent than with the *m*-hydroxymethyl and *o*-hydroxymethyl derivatives (Table 6).

In order to explore the scope of our reaction conditions, the reactivity of 2-methyl-3-buten-2-ol and 3-phenyl-2-propen-1-ol were assessed: reactions with *p*-tolylboronic acid were implemented under microwave heating at 140 °C

for 1.5 hours, using alternative allyl alcohols instead of methallyl alcohol. Alkenes **19** and **20**, respectively, were obtained in moderate to good yields (Table 7).

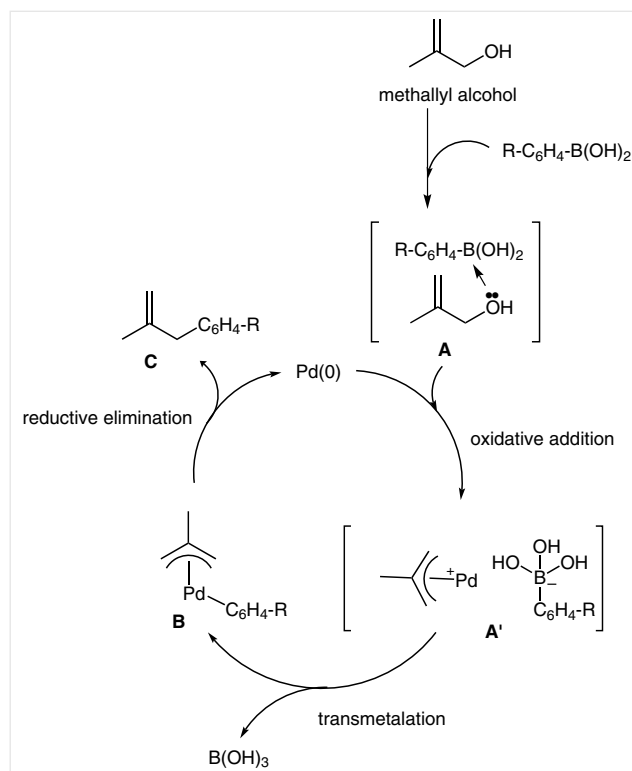
Table 7 Cross-Coupling Reactions of *p*-Tolylboronic Acid with Other Allyl Alcohols^a

Entry	Alcohol	Product	Yield (%)
1		19	46
2		20	94

^a Reaction conditions (a): *p*-tolylboronic acid (1.2 equiv), Cs₂CO₃ (2 equiv), Pd(OAc)₂ (0.5 mol%), Xantphos (2 mol%), air, MW, 140 °C, 1.5 h.

These results suggest that this kind of cross-coupling reaction under our reaction conditions could be easily expanded to other allyl alcohols.

Based on our experimental results and previous studies, a mechanism is suggested. First, allyl alcohol activated by coordination of the hydroxy group with the arylboronic acid (**A**) undergoes oxidative addition to palladium(0) through the allyl bond, to provide a cationic π -allylpalladi-



Scheme 3 Plausible catalytic cycle mechanism

um intermediate (**A'**). Then, this complex undergoes transmetalation to give diorganopalladium complex **B**. Reductive elimination finally affords the coupled product **C** (Scheme 3).⁷

In conclusion, we have developed an easy and environmentally friendly way to synthesize 2-methylallyl alkenes via cross-coupling reactions between 2-methyl-2-propen-1-ol and various arylboronic acids. Firstly, this study has shown that no additive solvent is required to carry out this kind of reaction. Moreover, the reaction offers greater atom economy than other classical cross-coupling reactions: the methylallyl alcohol used as a solvent can be recycled for further cross-coupling reactions; very low amounts of palladium (0.05 mol%) are sufficient to catalyze the reaction (Table 4, entry 4), even if 0.5 mol% of palladium is used under the optimized conditions. Secondly, we have shown that this new process exhibits a high functional group tolerance, being reproducible for a wide range of arylboronic acids (such as those with a hydroxymethyl group that constitute a real challenge). These outcomes open up new prospects for the formation of carbon–carbon bonds in general (since the hydroxy group is much less toxic and more accessible than halide groups), and the synthesis of terminal alkenes in particular. Complementary studies to explore this original mechanism are ongoing.

TLC was performed on Merck aluminum plates (5 × 10 cm) coated with silica gel 60 F₂₅₄ (0.2-mm layer), using an appropriate solvent. Melting points were determined in capillary tubes using a Büchi B-540 melting point apparatus. ¹H NMR and ¹³C NMR spectra were recorded in CDCl₃ or DMSO-*d*₆, with tetramethylsilane (TMS) as an internal reference using a Bruker ARX 200 spectrometer (operating at 200 MHz for ¹H NMR and 50 MHz for ¹³C NMR), a Bruker Avance III NanoBay 300-MHz spectrometer (operating at 300 MHz for ¹H NMR and 75 MHz for ¹³C NMR), and a Bruker Avance III NanoBay 400-MHz spectrometer (operating at 400 MHz for ¹H NMR and 101 MHz for ¹³C NMR) at the Service Interuniversitaire de RMN de la Faculté de Pharmacie de Marseille or the Spectropole de la Faculté des Sciences site Saint-Jérôme. ¹H NMR chemical shifts are quoted in parts per million as δ downfield from TMS (δ 0.00) as an internal standard, and the ¹³C NMR chemical shifts were referenced to the solvent peaks: CDCl₃ (76.9 ppm) or DMSO-*d*₆ (39.6 ppm). Coupling constants (*J* values) are given in hertz. NMR multiplicities are abbreviated as follows: *s* (singlet), *d* (doublet), *t* (triplet), *q* (quartet) and *m* (a more complex multiplet or overlapping multiplets). Microwave-assisted Suzuki–Miyaura cross-coupling reactions were performed in a monomode microwave oven (Biotage Initiator microwave oven using 10–20-mL or 2–5-mL sealed vials; temperatures were measured with an IR sensor and reaction times given as hold times). Elemental analysis and mass spectra, run on an API-QqTOF mass spectrometer, were carried out at the Spectropole de la Faculté des Sciences site Saint-Jérôme. All commercial reagents were used without purification.

(2-Methylallyl)benzene Derivatives 1–20

General Procedure for Reaction Conditions (a)

Conditions (a): sealed reactor, air, MW, 140 °C, 1.5 h.

A solution of 2-methyl-2-propen-1-ol (5 mL), a boronic acid (4.1 mmol, 1.2 equiv), Pd(OAc)₂ (3.8 mg, 0.017 mmol, 0.005 equiv), Xantphos (38 mg, 0.068 mmol, 0.02 equiv) and Cs₂CO₃ (2.3 g, 7 mmol, 2 equiv) was stirred in a sealed vial for 1.5 h at 140 °C, under microwave irradiation. Then, the solid residue was removed by filtration, and the filtrate was purified by distillation to obtain the alkene product.

General Procedure for Reaction Conditions (b)

Conditions (b): sealed reactor, air, MW, 120 °C, 1 h.

A solution of 2-methyl-2-propen-1-ol (5 mL), a boronic acid (4.1 mmol, 1.2 equiv), Pd(OAc)₂ (3.8 mg, 0.017 mmol, 0.005 equiv), Xantphos (38 mg, 0.068 mmol, 0.02 equiv) and Cs₂CO₃ (2.3 g, 7 mmol, 2 equiv) was stirred in a sealed vial for 1 h at 120 °C, under microwave irradiation. Then, the solid residue was removed by filtration, and the filtrate was purified by distillation to obtain the alkene product.

General Procedure for Reaction Conditions (c)

Conditions (c): air, 100 °C, 12 h.

A solution of 2-methyl-2-propen-1-ol (5 mL), a boronic acid (4.1 mmol, 1.2 equiv), Pd(OAc)₂ (3.8 mg, 0.017 mmol, 0.005 equiv), Xantphos (38 mg, 0.068 mmol, 0.02 equiv) and Cs₂CO₃ (2.3 g, 7 mmol, 2 equiv) was stirred in a sealed vial for 12 h at 100 °C. Then, the solid residue was removed by filtration, and the filtrate was purified by distillation to obtain the alkene product.

General Procedure for Reaction Conditions (d)

Conditions (d): sealed reactor, air, MW, 140 °C, 1.5 h; 2 steps.

A solution of 2-methyl-2-propen-1-ol (6 mL), Pd(OAc)₂ (7.6 mg, 0.034 mmol, 0.005 equiv), Xantphos (76 mg, 0.136 mmol, 0.02 equiv) and Cs₂CO₃ (2.3 g, 7 mmol, 1 equiv) was stirred in a sealed vial for 0.5 h at 140 °C, under microwave irradiation. A boronic acid (8.2 mmol, 1.2 equiv) was added to the reaction mixture which was then stirred in a sealed vial for 1 h at 140 °C, under microwave irradiation. Then, the solid residue was removed by filtration, and the filtrate was purified by distillation to obtain the alkene product.

(2-Methylallyl)benzene (1)¹⁴

Obtained from phenylboronic acid (500 mg) using method (a), as a colorless oil; yield: 450 mg (88%); bp 178 °C/760 torr.

¹H NMR (400 MHz, CDCl₃): δ = 7.33–7.20 (m, 5 H), 4.83 (s, 1 H), 4.76 (s, 1 H), 3.28 (s, 2 H), 1.64 (s, 3 H).

¹³C NMR (101 MHz, CDCl₃): δ = 142.3 (C), 139.8 (C), 128.9 (2 CH), 128.3 (2 CH), 126.1 (CH), 111.9 (CH₂), 44.7 (CH₂), 22.1 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₀H₁₂: 132.0939; found: 132.0984.

1-Methyl-2-(2-methylallyl)benzene (2)^{7a}

Obtained from *o*-tolylboronic acid (623 mg) using method (a), as a colorless oil; yield: 570 mg (86%); bp 156 °C/760 torr.

¹H NMR (200 MHz, CDCl₃): δ = 7.15 (s, 4 H), 4.83 (s, 1 H), 4.54 (s, 1 H), 3.33 (s, 2 H), 2.29 (s, 3 H), 1.76 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 144.2 (C), 137.9 (C), 136.8 (C), 130.1 (CH), 129.8 (CH), 126.3 (CH), 125.8 (CH), 111.6 (CH₂), 41.8 (CH₂), 22.7 (CH₃), 19.4 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₁H₁₄: 146.1096; found: 146.1458.

1-Methyl-3-(2-methylallyl)benzene (3)

Obtained from *m*-tolylboronic acid (623 mg) using method (b), as a colorless oil; yield: 490 mg (74%); bp 148 °C/760 torr.

¹H NMR (200 MHz, CDCl₃): δ = 7.25–6.89 (m, 4 H), 4.82 (s, 1 H), 4.75 (s, 1 H), 3.30 (s, 2 H), 2.35 (s, 3 H), 1.69 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 145.3 (C), 139.7 (C), 137.8 (C), 129.7 (CH), 128.2 (CH), 126.8 (CH), 126.0 (CH), 111.8 (CH₂), 44.6 (CH₂), 22.1 (CH₃), 21.4 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₁H₁₄: 146.1096; found: 146.1458.

1-Methyl-4-(2-methylallyl)benzene (4)^{7a}

Obtained from *p*-tolylboronic acid (557 mg) using method (a) [yield: 600 mg (100%)], or from 2,4,6-tri-*p*-tolyl-1,3,5,2,4,6-trioxatriborinane (1450 mg) using method (a), as a colorless oil; yield: 600 mg (100%); bp 177 °C/760 torr.

¹H NMR (200 MHz, CDCl₃): δ = 7.10 (s, 4 H), 4.80 (s, 1 H), 4.74 (s, 1 H), 3.29 (s, 2 H), 2.34 (s, 3 H), 1.69 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 145.4 (C), 136.7 (C), 135.5 (C), 129.0 (2 CH), 128.8 (2 CH), 111.7 (CH₂), 44.3 (CH₂), 22.1 (CH₃), 21.1 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₁H₁₄: 146.1096; found: 146.1141.

1-Bromo-2-(2-methylallyl)benzene (5)

Obtained from 2-bromophenylboronic acid (823 mg) using method (b), as a colorless oil; yield: 700 mg (81%); bp 157 °C/760 torr.

¹H NMR (200 MHz, CDCl₃): δ = 7.68–6.76 (m, 4 H), 4.98 (s, 1 H), 4.90 (s, 1 H), 3.46 (s, 2 H), 1.76 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 143.5 (C), 142.3 (C), 139.2 (C), 132.8 (CH), 130.9 (CH), 127.3 (CH), 126.9 (CH), 112.4 (CH₂), 43.9 (CH₂), 22.6 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₀H₁₁Br: 210.0044; found: 210.0078.

1-Bromo-4-(2-methylallyl)benzene (6)

Obtained from 4-bromophenylboronic acid (823 mg) using method (a), as a colorless oil; yield: 800 mg (92%); bp 158 °C/760 torr.

¹H NMR (200 MHz, CDCl₃): δ = 7.41 (d, *J* = 8.3 Hz, 2 H), 7.07 (d, *J* = 8.4 Hz, 2 H), 5.07 (s, 1 H), 4.95 (s, 1 H), 4.02 (s, 2 H), 1.86 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 141.3 (C), 138.7 (C), 131.3 (2 CH), 130.7 (2 CH), 119.9 (C), 115.2 (CH₂), 49.6 (CH₂), 22.0 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₀H₁₁Br: 210.0044; found: 210.0396.

1-(2-Methylallyl)-2-nitrobenzene (7)

Obtained from 2-nitrophenylboronic acid (684 mg) using method (c), as an orange oil; yield: 670 mg (92%); bp 171 °C/760 torr.

¹H NMR (200 MHz, CDCl₃): δ = 7.78 (m, 4 H), 4.96 (s, 1 H), 4.85 (s, 1 H), 3.86 (s, 2 H), 1.74 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 148.2 (C), 142.3 (C), 137.4 (C), 134.6 (CH), 129.3 (CH), 123.5 (2 CH), 111.9 (CH₂), 73.8 (CH₂), 19.5 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ for C₁₀H₁₁NO₂: 177.0790; found: 177.0834.

1-(2-Methylallyl)-3-nitrobenzene (8)

Obtained from 3-nitrophenylboronic acid (684 mg) using method (a), as a yellow oil; yield: 550 mg (76%); bp 144 °C/760 torr.

¹H NMR (200 MHz, CDCl₃): δ = 8.05 (s, 1 H), 8.11–7.38 (m, 3 H), 4.88 (s, 1 H), 4.75 (s, 1 H), 3.41 (s, 2 H), 1.68 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 148.3 (C), 143.5 (C), 141.8 (C), 135.1 (CH), 129.1 (CH), 123.7 (CH), 121.3 (CH), 113.3 (CH₂), 44.1 (CH₂), 22.0 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₀H₁₁NO₂: 177.0790; found: 177.1155.

1-(2-Methylallyl)-4-nitrobenzene (9)

Obtained from 4-nitrophenylboronic acid (684 mg) using method (a), as an orange oil; yield: 500 mg (70%); bp 170 °C/760 torr.

¹H NMR (200 MHz, CDCl₃): δ = 8.14 (d, *J* = 8.7 Hz, 2 H), 7.34 (d, *J* = 8.5 Hz, 2 H), 4.88 (s, 1 H), 4.74 (s, 1 H), 3.41 (s, 2 H), 1.67 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 147.6 (C), 146.6 (C), 143.4 (C), 129.7 (2 CH), 123.6 (2 CH), 113.4 (CH₂), 44.3 (CH₂), 22.1 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₀H₁₁NO₂: 177.0790; found: 177.1153.

4-(2-Methylallyl)-1,1'-biphenyl (10)¹⁵

Obtained from 1,1'-biphenyl-4-ylboronic acid (812 mg) using method (a), as a colorless oil; yield: 800 mg (94%); bp 225 °C/760 torr.

¹H NMR (200 MHz, CDCl₃): δ = 7.67–7.27 (m, 9 H), 4.88 (s, 1 H), 4.82 (s, 1 H), 3.39 (s, 2 H), 1.75 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 141.3 (C), 141.1 (C), 139.1 (C), 138.9 (C), 129.4 (s, 2 CH), 128.8 (2 CH), 127.3 (CH), 127.2 (2 CH), 127.1 (2 CH), 112.1 (CH₂), 44.3 (CH₂), 22.2 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₆H₁₆: 208.1252; found: 208.1615.

2-(2-Methylallyl)benzotrile (11)

Obtained from 2-cyanophenylboronic acid (602 mg) using method (c), as a light yellow oil; yield: 440 mg (68%); bp 160 °C/760 torr.

¹H NMR (200 MHz, CDCl₃): δ = 7.79–7.25 (m, 4 H), 4.88 (s, 1 H), 4.68 (s, 1 H), 3.54 (s, 2 H), 1.73 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 143.6 (2 C), 143.0 (2 C), 132.8 (CH), 132.7 (CH), 130.1 (CH), 126.8 (CH), 113.3 (CH₂), 42.6 (CH₂), 22.3 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₁H₁₁N: 157.0891; found: 157.0937.

3-(2-Methylallyl)benzotrile (12)

Obtained from 3-cyanophenylboronic acid (602 mg) using method (a), as a light yellow oil; yield: 550 mg (85%); bp 152 °C/760 torr.

¹H NMR (200 MHz, CDCl₃): δ = 7.74–7.31 (m, 4 H), 4.86 (s, 1 H), 4.72 (s, 1 H), 3.33 (s, 2 H), 1.65 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 143.6 (2 C), 141.2 (2 C), 133.5 (CH), 132.2 (CH), 130.0 (CH), 129.1 (CH), 113.2 (CH₂), 44.0 (CH₂), 22.0 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₁H₁₁N: 157.0891; found: 157.0964.

4-(2-Methylallyl)benzotrile (13)^{7c}

Obtained from 4-cyanophenylboronic acid (602 mg) using method (a), as a colorless oil; yield: 612 mg (95%); bp 181 °C/760 torr.

¹H NMR (200 MHz, CDCl₃): δ = 7.58 (d, *J* = 8.2 Hz, 2 H), 7.29 (d, *J* = 8.2 Hz, 2 H), 4.86 (s, 1 H), 4.72 (s, 1 H), 3.36 (s, 2 H), 1.66 (s, 3 H).

¹³C NMR (50 MHz, CDCl₃): δ = 145.4 (2 C), 143.6 (2 C), 132.2 (2 CH), 129.7 (2 CH), 113.2 (CH₂), 44.6 (CH₂), 22.1 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₁H₁₁N: 157.0891; found: 157.0840.

Anal. Calcd for C₁₁H₁₁N (157.0891): C, 84.04; H, 7.05; N, 8.91. Found: C, 83.78; H, 7.05; N, 9.11.

1-(2-Methylallyl)-4-vinylbenzene (14)¹⁶

Obtained from 4-vinylphenylboronic acid (607 mg) using method (a), as a slight yellow oil; yield: 500 mg (77%); bp 170 °C/760 torr.

¹H NMR (200 MHz, CDCl₃): δ = 7.36 (d, *J* = 8.1 Hz, 2 H), 7.17 (d, *J* = 8.1 Hz, 2 H), 6.72 (dd, *J* = 17.6, 10.9 Hz, 1 H), 5.73 (d, *J* = 17.6 Hz, 1 H), 5.22 (d, *J* = 10.9 Hz, 1 H), 4.83 (s, 1 H), 4.75 (s, 1 H), 3.32 (s, 2 H), 1.69 (s, 3 H).

¹³C NMR (75 MHz, CDCl₃): δ = 142.3 (C), 139.5 (C), 136.7 (CH), 135.5 (C), 129.1 (2 CH), 126.2 (2 CH), 113.1 (CH₂), 112.0 (CH₂), 44.4 (CH₂), 22.1 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₂H₁₄: 158.1096; found: 158.1140.

1,4-Bis(2-methylallyl)benzene (15)

Obtained from 1,4-phenylenediboronic acid (150 mg) using method (a), as a colorless oil; yield: 130 mg (77%); bp 158 °C/760 torr.

¹H NMR (200 MHz, CDCl₃): δ = 7.11 (s, 4 H), 4.81 (s, 2 H), 4.74 (s, 2 H), 3.30 (s, 4 H), 1.68 (s, 6 H).

¹³C NMR (75 MHz, CDCl₃): δ = 142.3 (2 C), 137.4 (2 C), 128.8 (4 CH), 112.0 (2 CH₂), 44.3 (2 CH₂), 22.1 (2 CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₄H₁₈: 186.1409; found: 186.1455.

[2-(2-Methylallyl)phenyl]methanol (16)

Obtained from 2-(hydroxymethyl)phenylboronic acid (1000 mg) using method (d), as an opalescent oil; yield: 900 mg (84%); bp 185 °C/760 torr.

¹H NMR (200 MHz, DMSO-*d*₆): δ = 8.09–6.61 (m, 4 H), 5.01 (t, *J* = 5.3 Hz, 1 H), 4.80 (s, 1 H), 4.56 (s, 1 H), 4.54 (d, *J* = 5.1 Hz, 2 H), 3.35 (s, 2 H), 1.69 (s, 3 H).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 144.7 (C), 141.0 (C), 136.7 (C), 128.5 (CH), 127.4 (CH), 127.0 (CH), 126.5 (CH), 111.9 (CH₂), 60.9 (CH₂), 40.5 (CH₂), 22.8 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₁H₁₄O: 162.1045; found: 162.1990.

[3-(2-Methylallyl)phenyl]methanol (17)

Obtained from 3-(hydroxymethyl)phenylboronic acid (1246 mg) using method (d), as a colorless oil; yield: 1100 mg (83%); bp 178 °C/760 torr.

¹H NMR (200 MHz, DMSO-*d*₆): δ = 7.41–6.92 (m, 4 H), 5.17 (t, *J* = 5.7 Hz, 1 H), 4.77 (s, 1 H), 4.73 (s, 1 H), 4.49 (d, *J* = 5.5 Hz, 2 H), 3.29 (s, 2 H), 1.62 (s, 3 H).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 145.2 (C), 143.0 (C), 139.6 (C), 128.4 (CH), 127.5 (CH), 127.2 (CH), 124.7 (CH), 112.3 (CH₂), 63.4 (CH₂), 44.4 (CH₂), 22.3 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₁H₁₄O: 162.1045; found: 162.1090.

[4-(2-Methylallyl)phenyl]methanol (18)

Obtained from 4-(hydroxymethyl)phenylboronic acid (1246 mg) using method (d), as a colorless oil; yield: 1200 mg (90%); bp 175 °C/760 torr.

¹H NMR (200 MHz, DMSO-*d*₆): δ = 7.25 (d, *J* = 7.8 Hz, 2 H), 7.13 (d, *J* = 7.9 Hz, 2 H), 5.14 (t, *J* = 5.7 Hz, 1 H), 4.76 (s, 1 H), 4.71 (s, 1 H), 4.47 (d, *J* = 5.9 Hz, 2 H), 3.27 (s, 2 H), 1.61 (s, 3 H).

¹³C NMR (50 MHz, DMSO-*d*₆): δ = 145.4 (C), 140.8 (C), 138.1 (C), 128.9 (2 CH), 127.0 (2 CH), 112.2 (CH₂), 63.3 (CH₂), 44.0 (CH₂), 22.2 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₁H₁₄O: 162.1045; found: 162.1090.

Anal. Calcd for C₁₁H₁₄O (162.1045): C, 81.44; H, 8.70. Found: C, 81.34; H, 8.73.

1-Methyl-4-(2-methyl-3-buten-2-yl)benzene (19)¹⁷

Obtained from *p*-tolylboronic acid (557 mg) using method (a), with 2-methyl-3-buten-2-ol instead of 2-methyl-2-propen-1-ol, as a slight yellow oil; yield: 300 mg (46%); bp 178 °C/760 torr.

¹H NMR (200 MHz, CDCl₃): δ = 7.77 (d, *J* = 8.6 Hz, 2 H), 6.97 (d, *J* = 8.6 Hz, 2 H), 6.00 (dd, *J* = 17.4, 10.7 Hz, 1 H), 5.10 (ddd, *J* = 14.0, 11.6, 0.9 Hz, 2 H), 3.86 (s, 3 H), 1.32 (s, 6 H).

¹³C NMR (63 MHz, CDCl₃): δ = 161.9 (2 C), 146.1 (CH), 136.7 (2 CH), 113.5 (2 CH), 110.9 (CH₂), 71.2 (C), 55.2 (2 CH₃), 29.4 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₂H₁₆: 160.1252; found: 160.1215.

1-Cinnamyl-4-methylbenzene (20)^{7h}

Obtained from *p*-tolylboronic acid (250 mg) using method (a), with 3-phenyl-2-propen-1-ol instead of 2-methyl-2-propen-1-ol, as a white oil; yield: 360 mg (94%).

¹H NMR (200 MHz, CDCl₃): δ = 7.35–7.11 (m, 9 H), 6.47 (d, *J* = 15.5 Hz, 1 H), 6.41–6.27 (m, 1 H), 3.52 (d, *J* = 6.3 Hz, 2 H), 2.34 (s, 3 H).

¹³C NMR (63 MHz, CDCl₃): δ = 137.5 (C), 137.0 (C), 135.7 (C), 130.8 (CH), 129.5 (CH), 129.2 (2 CH), 128.6 (2 CH), 128.5 (2 CH), 127.0 (CH), 126.1 (2 CH), 38.9 (CH₂), 21.0 (CH₃).

HRMS (ESI+): *m/z* [M]⁺ calcd for C₁₆H₁₆: 208.1252; found: 208.1315.

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