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Palladium-Catalyzed Suzuki Coupling of Propargylic Alcohols with Boronic Acids under Ambient Conditions

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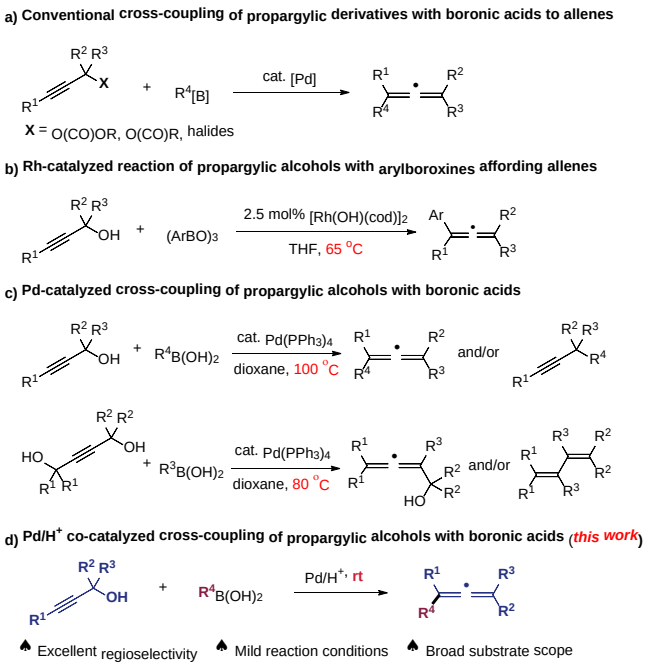
Summary of main observation and conclusion A highly efficient palladium-catalyzed direct Suzuki coupling of propargylic alcohols with organoboronic acids to synthesize tri- and tetra-substituted allenes has been developed under mild reaction conditions. Many useful functional groups are tolerated in this process with high to excellent yields. Preliminary biological studies showed that several tri- and tetra-substituted allenes exhibited potent anti-diabetic activities.

Background and Originality Content

Allenes are important synthetic building blocks in organic synthesis and many natural products and pharmaceutical drugs contain allene motifs.[1,2] Consequently, many studies have been focused on the synthesis of different types of allenes.[3] Transition metal-catalyzed cross-coupling reactions are powerful tools for C-C bond formation.[4] The Suzuki coupling reaction has been widely exploited in last few decades.[5] Pd-catalyzed Suzuki coupling of propargylic compounds with organoboronic acids is one of the most straightforward approaches for allene synthesis.[6] However, reactive substrates bearing a good leaving group such as propargylic halides, esters or carbonates were required in these protocols (Scheme 1a).[6]

Suzuki coupling of propargylic alcohols has less been reported due to the difficulty encountered in the step of oxidative addition with a transition metal catalyst.[7-9] Dou and co-workers reported Rh-catalyzed cross-coupling of propargylic alcohols with arylboroxines affording allenes via S_N2'-type mechanism (Scheme 1b).[7] Yoshida and Ihara found the Pd-catalyzed direct coupling of propargylic alcohols with arylboronic acids affording allenes and/or alkynes could be achieved at 100 °C (Scheme 1c, up).[6j] Cherburn and co-workers developed Pd-catalyzed direct coupling of 2-butynyl 1,4-diols with boronic acids generating allenes and/or dienes at 80 °C (Scheme 1c, down).[6k] Recently, our group put forward a new concept of utilizing a catalytic amount of Brønsted acid to form a transient leaving group from the hydroxy group, and successfully achieved the atom-economic synthesis of 2,3-allenoates and 2,3-allenoic acids via the carboxylation with CO.[8] With our goal of developing more efficient methods in the synthesis of allenes with simple starting substrates, we propose a direct Suzuki coupling of organoboronic acids with propargylic alcohols under mild conditions under the co-catalysis of Pd(0) and an organic acid (Scheme 1d).

Scheme 1 Transition metal-catalyzed cross-coupling to synthesize allenes



Results and Discussion

We began our investigation with the propargylic alcohol **1a** which bears one phenyl and one methyl group on the α-carbon and phenylboronic acid **2a** to identify the ligands for the reaction at room temperature (Scheme 2). We initially used *o*-(diphenylphosphino) benzaldehyde (**L1**), which performed efficiently in the system of propargylic carbonates.[6g] Unfortunately, 94% of propargylic alcohol **1a** was recovered and the desired

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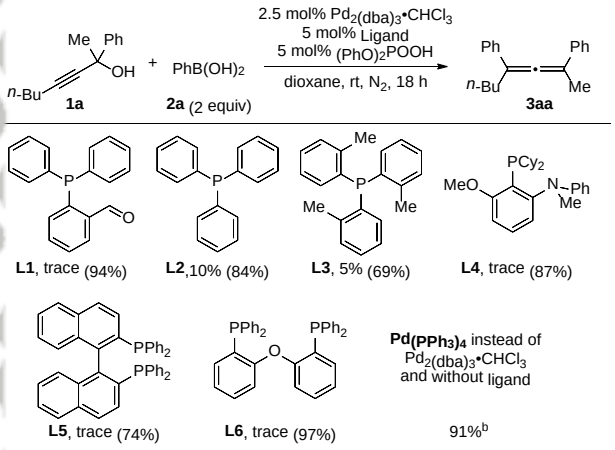
product **3aa** was not formed. Triphenylphosphine (**L2**) was then employed as the ligand and the desired allene product **3aa** was formed in only 10% yield. Tri(*o*-tolyl)phosphine (**L3**) provided 5% yield of **3aa** with 69% recovery of **1a**.[6h,6i] Zheda-phos (**L4**) also failed to give the allene product.[9] We next investigated the effect of bidentated phosphine ligand. However, both BINAP (**L5**) and DPEPhos (**L6**) could not afford allene product **3aa**. To our surprise, using of $Pd(PPh_3)_4$ instead of $Pd_2(dba)_3{\cdot}CHCl_3$ could give 91% yield allene product **3aa** without any recovery of **1a**.

Scheme 2 Ligand Screening[a]

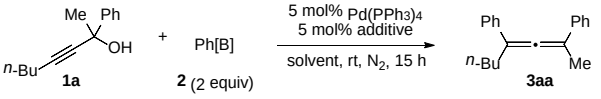


[a] The reaction was conducted with 0.2 mmol of **1a**, 0.4 mmol of **2a**, 2.5 mol% of $Pd_2(dba)_3{\cdot}CHCl_3$, 5 mol% ligand, and 5 mol% of $(PhO)_2POOH$ in 1.0 mL of anhydrous dioxane at rt for 18 h under N_2 atmosphere. The yield and recovery were determined by ^1H NMR analysis, and the recovery of **1a** is shown in the parentheses. [b] 5 mol% $Pd(PPh_3)_4$ was used and reaction time is 13 h.

After identifying $Pd(PPh_3)_4$ as the best catalyst, other reaction parameters were then studied (Table 1). Only 10% of desired allene product was observed without adding $(PhO)_2POOH$ as additive (entry 1). And no reaction occurred when 4 equiv of water were added as the additive (entry 3). Next, solvent was found to be crucial for this Suzuki coupling process. Moderate efficiency was observed in THF, DME, and Toluene (entries 4-6), while no reaction occurred in CH_3CN (entry 7). The yield dropped to 60% when reducing the amount of $PhB(OH)_2$ to 1.5 equiv (entry 8). We also investigated the reactivity of other boron reagents (entries 9–11): PhBpin, $(PhBO)_3$, and $PhBF_3K$ failed to afford the desired product. Thus, optimal conditions have been defined as 5 mol% of $Pd(PPh_3)_4$ and 5 mol% of $(PhO)_2POOH$ in dioxane at room temperature under N_2 atmosphere.

With the optimized condition in hand, we examined the scope of boronic acids with propargylic alcohol **1a**. As shown in Scheme 3, a wide range of aryl boronic acids with different substituents at different positions all reacted smoothly with **1a** to form the corresponding tetrasubstituted allene products **3** with good to excellent efficiency. The reaction is amenable to both electron-withdrawing and electron-donating groups. Aryl boronic acid bearing *ortho*-, *meta*-, or *para*-methyl substitutions gave the products in high yields under optimal reaction conditions (**3ab**-**3ad**). Other electron-donating substituents such as *tert*-butyl and methoxy also afforded allene products in good yields (**3ae**, **3ah**, and **3ai**). The halo-substituted (F, Cl) aryl boronic acid also worked (**3af** and **3ag**). The electron-withdrawing groups such as nitro, cyano, acetyl, formyl in aryl were all tolerated under ambient conditions (**3aj**-**3am**). The useful functional groups such as trifluoromethyl and ester afforded the corresponding allenes successfully (**3an** and **3ao**). 4-Biphenylboronic acid and 2-naphthyl boronic acid were also suitable (**3ap** and **3aq**). Heterocycles such as furan and thiophene may also be tolerated with 80% and 75% yields, respectively (**3ar** and **3as**).

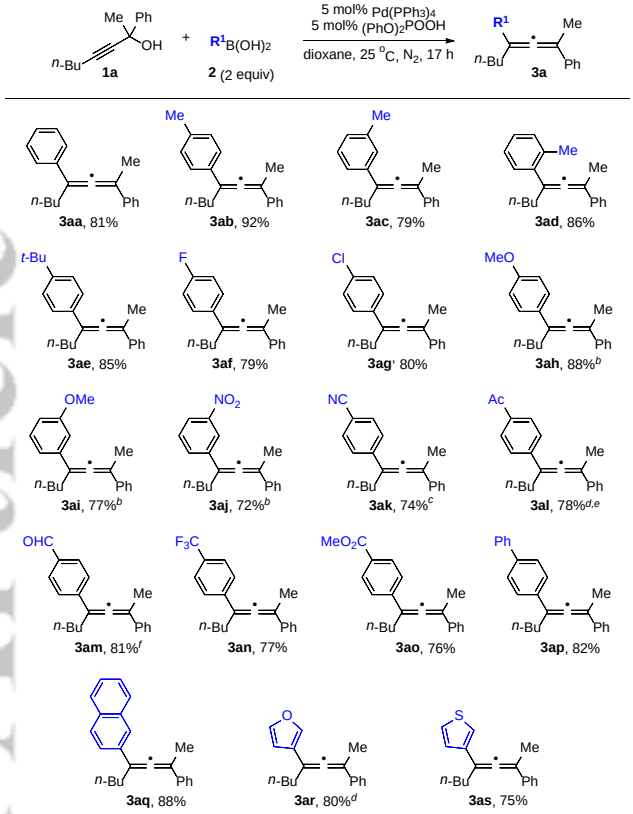
Table 1 Optimization of the reaction conditions[a]



entry	Solvent	additive	Ph[B]	NMR yield of **3aa** (%)	recovery of **1a** (%)
1[b]	dioxane	none	$PhB(OH)_2$	10	90
2[b]	dioxane	$(PhO)_2POOH$	$PhB(OH)_2$	91	trace
3[b]	dioxane	4 equiv H_2O	$PhB(OH)_2$	trace	100
4	THF	$(PhO)_2$ POOH	$PhB(OH)_2$	44	38
5	DME	$(PhO)_2$ POOH	$PhB(OH)_2$	38	38
6	Toluene	$(PhO)_2$ POOH	$PhB(OH)_2$	44	24
7	MeCN	$(PhO)_2$ POOH	$PhB(OH)_2$	trace	85
8[c]	dioxane	$(PhO)_2$ POOH	$PhB(OH)_2$	60	16
9[d]	dioxane	$(PhO)_2$ POOH	PhBpin	trace	98
10[d]	dioxane	$(PhO)_2$ POOH	$(PhBO)_3$	trace	91
11[d]	dioxane	$(PhO)_2$ POOH	$PhBF_3K$	trace	86

[a] The reaction was conducted with 0.2 mmol of **1a**, 0.4 mmol of **2**, 5 mol% of $Pd(PPh_3)_4$, and 5 mol% of additive in 1.0 mL of anhydrous solvent at rt for 15 h under N_2 atmosphere. The yield and recovery were determined by ^1H NMR analysis. [b] Reaction time is 13 h. [c] 1.5 equiv $PhB(OH)_2$ was used. [d] Reaction time is 18.5 h.

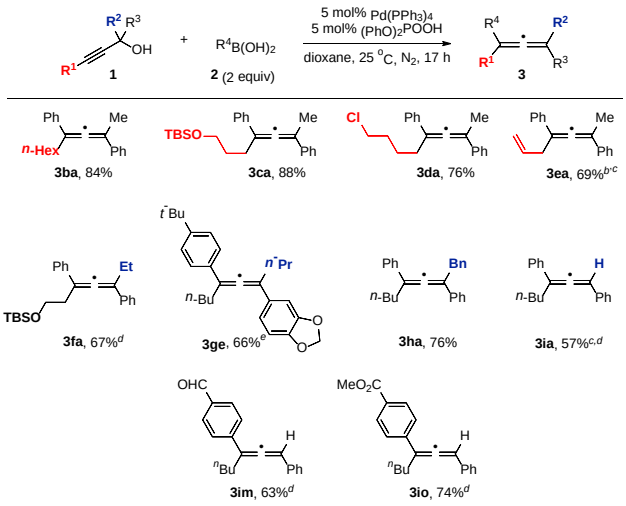
Scheme 3 Scope of boronic acids with **1a**[a]



[a] The reaction was conducted with 1.0 mmol of **1a**, 2.0 mmol of **2**, 5 mol% of $Pd(PPh_3)_4$, and 5 mol% of $(PhO)_2POOH$ in 5.0 mL of anhydrous dioxane at 25 °C for 17 h under N_2 atmosphere. [b] Reaction time is 36 h. [c] The reaction was conducted at 40 °C. [d] 10 mol % of $(PhO)_2POOH$ was used. [e] Reaction time is 24 h. [f] Reaction time is 19 h.

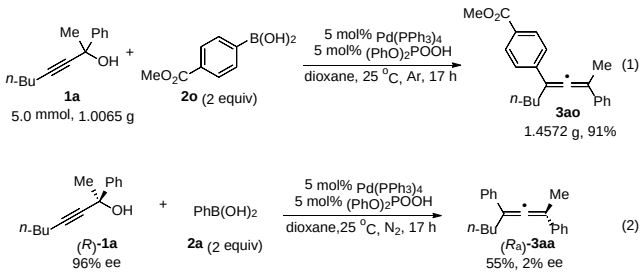
As shown in Scheme 4, a wide range of propargylic alcohols may participate in the efficient process to form the desired allenes. Propargylic alcohols with different chain lengths of alkyl groups did not affect the yield under standard conditions (**3ba**). Alkyl chain with different functional groups, such as silyl-protected alcohol (**3ca** and **3fa**), halide (**3da**) and vinyl (**3ea**) were well tolerated in this transformation. Ethyl, propyl and benzyl substitutions on the α-carbon of propargylic alcohol performed well to afford corresponding allenes (**3fa**, **3ge**, and **3ha**). It is worth noting that secondary propargylic alcohol **1i** also worked with different arylboronic acids to afford trisubstituted allenes with moderate to good yields (**3ia**, **3im** and **3io**).

Scheme 4 Substrate scope[a]



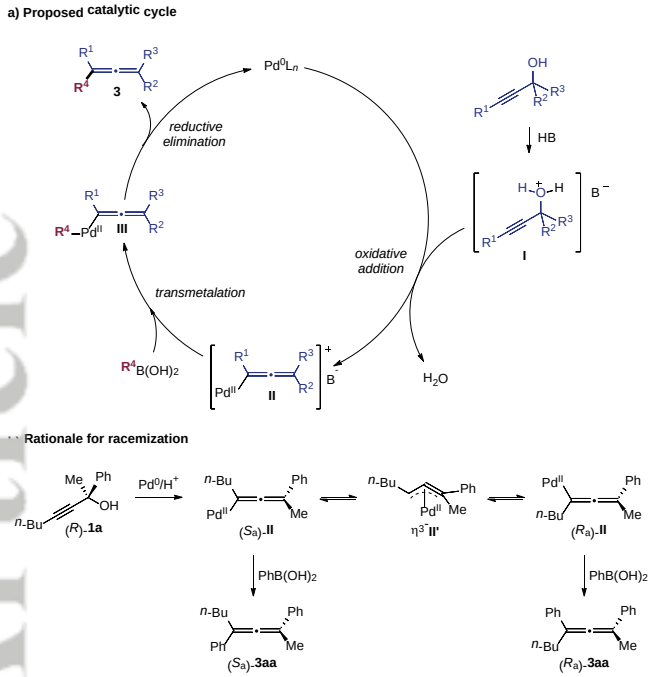
[a] The reaction was conducted with 1.0 mmol of **1a**, 2.0 mmol of **2**, 5 mol% of $Pd(PPh_3)_4$, and 5 mol% of $(PhO)_2POOH$ in 5.0 mL of anhydrous dioxane at 25 °C for 17 h under N_2 atmosphere. [b] 10 mol % of $(PhO)_2POOH$ was used. [c] Reaction time is 36 h. [d] The reaction was conducted at 40 °C. [e] Reaction time is 39.5 h.

To demonstrate the practicality of the efficient Suzuki coupling process, we carried out the reaction for gram scale synthesis of **3ao**: 1.4572 g **3ao** was afforded with 91% yield under standard conditions (eq 1). We studied the reaction of optically active propargylic alcohols[10] with boronic acid **2a** under the standard reaction conditions leading to the formation of (*R*)-**3aa** in 2% ee (eq 2). The Pd(0) would undergo S_N2'-type oxidative addition with propargylic alcohol (*R*)-**1a** in the presence of H^+ in *anti*-stereospecific manner to give intermediate (S_a)-**II,** which would racemize via the η^3-propargylic/allenylpalladium (**II'**) resulting in the formation of **3aa** with low enantioselectivity (Scheme 5b).[11]



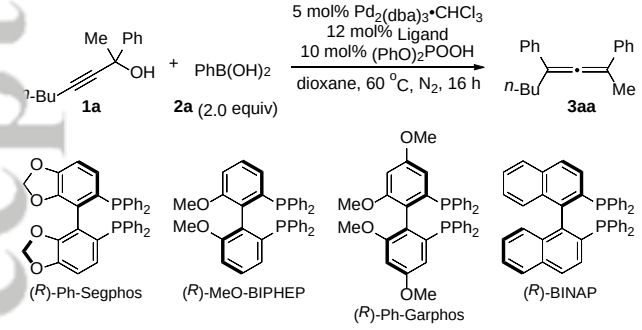
A possible catalytic cycle is proposed in Scheme 5a. The reaction of propargylic alcohol with Brønsted acid (HB) would yield the oxonium ion **I**, which would easily undergo oxidative addition reaction with Pd(0) to produce the allenylpalladium intermediate **II**. Here the racemization would occur. Subsequently, intermediate **II** would undergo transmetalation with the boronic acid to form the allenyl aryl palladium intermediate **III**, which would result in the formation of allenes and regenerate of Pd(0) species to complete the catalytic cycle via reductive elimination.

Scheme 5 The proposed mechanism



We tried to realize the catalytic asymmetric synthesis of chiral tetrasubstituted allenes. So we screened some chiral ligands at 60 °C (Table 2). 86% of propargylic alcohol **1a** was recovered when we use (*R*)-Ph-Segphos as ligand (Entry 1). Other ligands, such as (*R*)-MeO-BIPHEP, (*R*)-Ph-Garphos and (*R*)-BINAP, also failed to afford the desired allene product **3aa** (Entries 2-4). We are still working on it.

Table 2 Chiral ligand screening[a]



entry	Ligand	NMR yield of **3aa** (%)	ee of **3aa** (%)	recovery of **1a** (%)
1	(*R*)-Ph-Segphos	/	/	86
2	(*R*)-MeO-BIPHEP	/	/	83
3	(*R*)-Ph-Garphos	/	/	89
4	(*R*)-BINAP	/	/	61

[a] The reaction was conducted with 0.1 mmol of **1a**, 0.2 mmol of **2a**, 5 mol% of $Pd_2(dba)_3$•$CHCl_3$, 12 mol% of Ligand, and 10 mol% of $(PhO)_2POOH$ in 1.0 mL of anhydrous dioxane at 60 °C for 16 h under N_2 atmosphere. The NMR yield and recovery were determined by ^1H NMR analysis.

Finally, the potential biological activities of the newly synthesized compounds were evaluated. We first examined the effect of the compounds on the secretion of glucagon-like peptide-1 (GLP-1), which is an attractive therapeutic target for type II diabetes. As shown in Table 3, **3aj**, **3da** and **3ha** markedly stimulated GLP-1 release in mouse intestinal cell line STC-1 at 100 μM, which were more effective than the positive control phorbol-12-myristate-13-acetate (PMA, 1 μM). Then the three compounds were further tested and the half maximal effective concentration (EC_{50}) was measured. Notably, **3da** possessed the most potent stimulatory activity with an EC_{50} of 1.6 μM, suggesting that it might be a promising anti-diabetic agent for further study.

Table 3 Stimulation of GLP-1 release in STC-1 cells

Compound	Relative activity (%)[a]	EC_{50} (μM)[b]
3aa	46.1	
3ab	66.5	
3ad	51.2	
3ae	44.5	
3aj	103.5	24.5±7.4
3al	5.9	
3an	51.5	
3ao	5.0	
3aq	80.1	
3ar	74.9	
3as	60.0	
3ba	37.9	
3ca	1.3	
3da	107.4	1.6±0.0
3ea	76.8	
3ha	127.8	> 50

[a] The concentration of the tested compounds was 100 μM. The level of GLP-1 was normalized to that in the presence of the positive control PMA (1μM). [b] EC_{50}s are presented as mean ± SD.

The anti-diabetic effect of the compounds was also evaluated by using another cell model. Since diabetic patients often have defect in glucose consumption by the peripheral tissues such as skeletal muscle, we used rat L6 myotube cells to investigate the effect of the compounds on the utilization of glucose. Intriguingly, **3ab**, **3ad**, **3ae**, **3aj**, **3an**, **3ao**, **3da** and **3ea** effectively stimulated glucose consumption at 100 μM, leading to more than 1.5-fold improvement over the vehicle control DMSO. While lowering the concentration to 30 μM, **3ad**, **3an** and **3ao** still exhibited good

activity (> 1.2-fold). Further investigations of their anti-diabetic activities and mechanisms are under way.

Table 4 Stimulation of glucose consumption in rat L6 myotube cells

Compound	Relative activity (%)[a]	
	30 μM	100 μM
3aa	100.7±2.2	127.2±7.6
3ab	119.8±3.3	161.5±8.0
3ad	123.2±1.3	168.4±6.1
3ae	108.1±2.3	157.9±4.0
3aj	104.3±6.6	157.6±4.4
3al	113.6±3.7	131.5±5.0
3an	120.9±2.5	170.5±3.2
3ao	120.4±1.1	151.7±5.1
3aq	109.8±4.0	139.6±2.0
3ar	101.5±6.2	103.0±1.2
3as	105.6±1.5	147.7±1.5
3ba	105.7±4.7	137.8±6.3
3ca	97.0±4.0	101.7±6.2
3da	102.7±5.9	153.1±1.9
3ea	108.1±5.1	155.0±3.0
3ha	105.3±2.9	96.1±4.3
DMSO[b]	100.0±5.5	
Metformin[c]	148.3±3.2	

[a] Data were normalized to that of the DMSO group and presented as mean ± SD. [b] The concentration of DMSO was 1%. [c] The concentration of metformin was 10 mM.

Conclusions

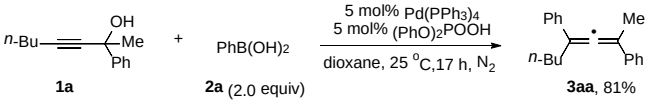
In conclusion, we have developed a general and highly efficient catalytic system for the Suzuki coupling of propargylic alcohols with boronic acids. Many functional groups are compatible under the very mild reaction conditions to afford trisubstituted and tetrasubstituted allenes facilely. Several newly synthesized compounds in this study displayed potent anti-diabetic activities. Further studies on the details of the reaction mechanism as well as the asymmetric protocol are in progress in our laboratory.

Experimental

General Information. NMR spectra were taken with an Agilent-400 spectrometer (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR, and 376 MHz for ^{19}F NMR) in $CDCl_3$. Chemical shifts were recorded in ppm in relative to the TMS in $CDCl_3$ and coupling constants were reported in Hz. All reactions were carried out in vial. $Pd(PPh_3)_4$ was purchased from J&K Chemicals and chembee; $PhB(OH)_2$ was purchased from bokachem Reagent Co; Petroleum ether (b.p. 60-90 °C) was purchased from Shanghai Titan Scientific Co., Ltd. 1,4-dioxane was dried over sodium wire with benzophenone as the indicator and distilled freshly before use. All the temperatures are referred to the Reaction Block used. NMR yield of allenes were determined by ^{1}H NMR analysis using dibromomethane as the internal standard. The starting propargylic alcohols were synthesized according to the reported procedures.[12]

1. Synthesis of allenes

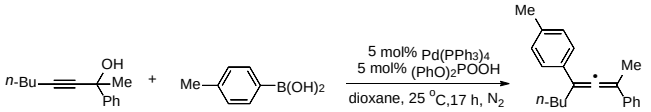
(1) Preparation of 2.4-diphenyl-2,3-octadiene (3aa, QAN-2-149)



1a **2a** (2.0 equiv) **3aa**, 81%

Typical Procedure: To an oven-dried 20 mL vial equipped with a stirring bar were added phenylboronic acid (243.9 mg, 2.0 mmol) and $(PhO)_2POOH$ (12.7 mg, 0.05 mmol). Then the vial was transferred to a glovebox with nitrogen atmosphere. After adding $Pd(PPh_3)_4$ (57.7 mg, 0.05 mmol), **1a** (202.6 mg, 1.0 mmol), and anhydrous dioxane (5 mL), the vial was capped with a Teflon lined lid, sealed with electrical tape, and transferred out of the glovebox. After stirring for 17 h in the reaction block at 25 °C, the reaction mixture were filtered through a short column silica gel (3 cm) eluted with ethyl acetate (20 mL). After removal of the solvent under vacuum, the crude product was analyzed by ^{1}H NMR with CH_2Br_2 (35 μL) as the internal standard: 77% NMR yield of **3aa** was formed based on ^{1}H NMR analysis. The residue was purified by column chromatography on silica gel to afford **3aa** (216.8 mg, 81%, 99% purity) as an oil [eluent: petroleum ether (200 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.43 (t, *J* = 7.4 Hz, 4 H, Ar-H), 7.34-7.25 (m, 4 H, Ar-H), 7.23-7.16 (m, 2 H, Ar-H), 2.55 (t, *J* = 7.6 Hz, 2 H, CH_2), 2.20 (s, 3 H, CH_3), 1.57 (quintet, *J* = 7.6 Hz, 2 H, CH_2), 1.48-1.34 (m, 2 H, CH_2), 0.91 (t, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 205.6, 137.3, 137.1, 128.41, 128.38, 126.7, 126.6, 126.1, 125.6, 107.8, 103.6, 30.1, 30.0, 22.6, 16.8, 14.0; **MS** (70 eV, EI) *m/z* (%): 263 (M^++1, 1.60), 262 (M^+, 7.01), 205 (100); **IR** (neat): *v* = 3026, 2955, 2925, 2859 1934, 1596, 1490, 1443, 1372, 1065, 1025 cm^{-1}; **HRMS** calcd for $C_{20}H_{22}$ [M^+]: 262.1722; found 262.1724.

(2) Preparation of 2-phenyl-4-(4-methylphenyl)-2,3-octadiene (3ab, QAN-5-120)

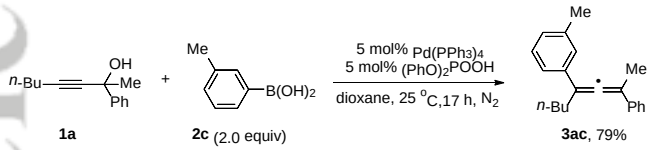


1a **2b** (2.0 equiv) **3ab**, 92%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.6 mg, 0.05 mmol), *p*-tolylboronic acid (271.6 mg, 2.0 mmol), $(PhO)_2POOH$ (12.5 mg, 0.05 mmol), **1a** (202.3 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3ab** (255.0 mg, 92%) as an oil [eluent: petroleum ether (200 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.44 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.34-7.24 (m, 4 H, Ar-H), 7.23-7.16 (m, 1 H, Ar-H), 7.11 (d, *J* = 7.6 Hz, 2 H, Ar-H), 2.52 (t, *J* = 7.4 Hz, 2 H, CH_2), 2.32 (s, 3 H, CH_3), 2.19 (s, 3 H, CH_3), 1.55 (quintet, *J* = 7.4 Hz, 2 H, CH_2), 1.45-1.33 (m, 2 H, CH_2), 0.90 (t, *J* = 7.4 Hz, 3 H,

CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 205.3, 137.4, 136.4, 134.0, 129.1, 128.3, 126.5, 126.0, 125.6, 107.6, 103.4, 30.1, 30.0, 22.6, 21.0, 16.9, 14.0; **MS** (70 eV, EI) *m/z* (%): 277 (M^++1, 3.31), 276 (M^+, 13.79), 219 (100); **IR** (neat): *v* = 3023, 2924, 2858, 1931, 1597, 1510, 1443, 1377, 1183, 1109, 1065, 1026 cm^{-1}; **HRMS** calcd for $C_{21}H_{24}$ [M^+]: 276.1878; found 276.1877.

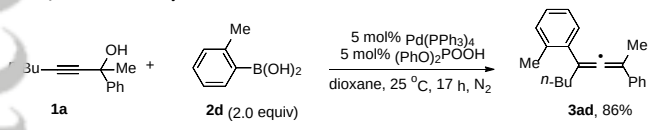
(3) Preparation of 2-phenyl-4-(3-methylphenyl)-2,3-octadiene (3ac, QAN-2-160)



1a **2c** (2.0 equiv) **3ac**, 79%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.9 mg, 0.05 mmol), *m*-tolylboronic acid (272.3 mg, 2.0 mmol), $(PhO)_2POOH$ (12.6 mg, 0.05 mmol), **1a** (202.3 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3ac** (232.5 mg, 79%, 91.5% purity) as an oil [eluent: petroleum ether (200 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.44 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.31 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.26-7.12 (m, 4 H, Ar-H), 7.01 (d, *J* = 7.2 Hz, 1 H, Ar-H), 2.62-2.48 (m, 2 H, CH_2), 2.32 (s, 3 H, CH_3), 2.20 (s, 3 H, CH_3), 1.62-1.50 (m, 2 H, CH_2), 1.47-1.33 (m, 2 H, CH_2), 0.90 (t, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 205.5, 137.9, 137.3, 137.0, 128.4, 128.3, 127.5, 126.7, 126.6, 125.6, 123.2, 107.8, 103.4, 30.11, 30.05, 22.6, 21.5, 16.8, 14.0; **MS** (70 eV, EI) *m/z* (%): 277 (M^++1, 2.50), 276 (M^+, 10.75), 219 (100); **IR** (neat): *v* = 3024, 2924, 2859, 1933, 1599, 1489, 1444, 1372, 1176, 1094, 1064 cm^{-1}; **HRMS** calcd for $C_{21}H_{24}$ [M^+]: 276.1878; found 276.1876.

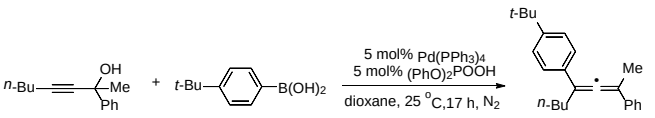
(4) Preparation of 2-phenyl-4-(2-methylphenyl)-2,3-octadiene (3ad, QAN-3-078)



1a **2d** (2.0 equiv) **3ad**, 86%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), *o*-tolylboronic acid (271.9 mg, 2.0 mmol), $(PhO)_2POOH$ (12.6 mg, 0.05 mmol), **1a** (201.9 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3ad** (236.5 mg, 86%) as an oil [eluent: petroleum ether (200 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.45-7.38 (m, 2 H, Ar-H), 7.34-7.26 (m, 3 H, Ar-H), 7.20-7.09 (m, 4 H, Ar-H), 2.54-2.33 (m, 5 H, CH_2 and CH_3), 2.15 (s, 3 H, CH_3), 1.55-1.44 (m, 2 H, CH_2), 1.43-1.33 (m, 2 H, CH_2), 0.89 (t, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 203.3, 138.1, 137.8, 135.8, 130.4, 128.2, 128.1, 126.7, 126.3, 125.74, 125.71, 106.7, 100.7, 34.0, 30.1, 22.5, 20.7, 17.1, 14.0; **MS** (70 eV, EI) *m/z* (%): 277 (M^++1, 1.60), 276 (M^+, 6.31), 219 (100); **IR** (neat): *v* = 3059, 2924, 2860, 1941, 1799, 1596, 1488, 1449, 1373, 1102, 1064, 1027 cm^{-1}; **HRMS** calcd for $C_{21}H_{24}$ [M^+]: 276.1878; found 276.1879.

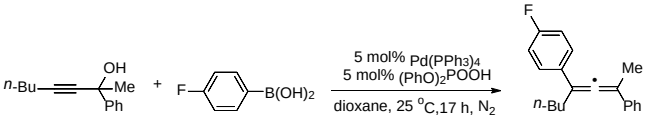
(5) Preparation of 2-phenyl-4-(4-*tert*-butylphenyl)-2,3-octadiene (3ae, QAN-2-164)



1a **2e** (2.0 equiv) **3ae**, 85%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), (4-(*tert*-butyl)phenyl)boronic acid (356.3 mg, 2.0 mmol), $(PhO)_2POOH$ (12.6 mg, 0.05 mmol), **1a** (202.0 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3ae** (270.6 mg, 85%) as a white solid [eluent: petroleum ether (200 mL)]; M.p. 64.3-68.4 °C (petroleum ether); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.48-7.42 (m, 2 H, Ar-H), 7.40-7.27 (m, 6 H, Ar-H), 7.24-7.15 (m, 1 H, Ar-H), 2.53 (t, *J* = 7.6 Hz, 2 H, CH_2), 2.19 (s, 3 H, CH_3), 1.65-1.54 (m, 2 H, CH_2), 1.50-1.38 (m, 2 H, CH_2), 1.31 (s, 9 H, 3 x CH_3), 0.90 (t, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 205.4, 149.7, 137.4, 134.0, 128.3, 126.5, 125.7, 125.6, 125.3, 107.5, 103.5, 34.4, 31.3, 30.1, 29.9, 22.7, 16.9, 14.0; **MS** (70 eV, EI) *m/z* (%): 318 (M^+, 2.39), 261 (100); **IR** (neat): *v* = 3033, 2954, 2923, 2860, 1928, 1713, 1602, 1494, 1437, 1271, 1180, 1106 cm^{-1}; Anal. Calcd. for $C_{24}H_{30}$: C: 90.51, H: 9.49; Found: C: 90.53, H: 9.67.

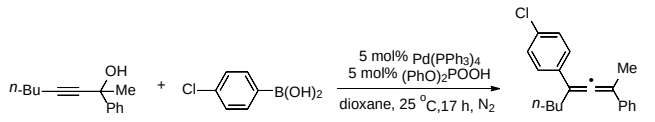
(6) Preparation of 2-phenyl-4-(4-fluorophenyl)-2,3-octadiene (3af, QAN-5-070)



1a **2f** (2.0 equiv) **3af**, 79%

Following **Typical Procedure** , the reaction of $Pd(PPh_3)_4$ (57.7 mg, 0.05 mmol), (4-fluorophenyl)boronic acid (280.2 mg, 2.0 mmol), $(PhO)_2POOH$ (12.5 mg, 0.05 mmol), **1a** (201.7 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3af** (220.8 mg, 79%) as an oil [eluent: petroleum ether (400 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.43 (d, *J* = 7.6 Hz, 2 H, Ar-H), 7.39-7.26 (m, 4 H, Ar-H), 7.20 (t, *J* = 7.2 Hz, 1 H, Ar-H), 6.98 (t, *J* = 8.6 Hz, 2 H, Ar-H), 2.58-2.42 (m, 2 H, CH_2), 2.20 (s, 3 H, CH_3), 1.58-1.50 (m, 2 H, CH_2), 1.46-1.35 (m, 2 H, CH_2), 0.91 (t, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 205.2 (d, *J* = 1.5 Hz), 161.8 (d, *J* = 244.9 Hz), 137.1, 133.0 (d, *J* = 3.2 Hz), 128.4, 127.5 (d, *J* = 7.9 Hz), 126.7, 125.6, 115.2 (*J* = 21.4 Hz), 107.0, 103.8, 30.2, 30.0, 22.6, 16.8, 13.9; **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -116.7; **MS** (70 eV, EI) *m/z* (%): 280 (M^+, 4.63), 190 (100); **IR** (neat): *v* = 3046, 2956, 2928, 2859, 1934, 1600, 1506, 1464, 1227, 1158, 1065 cm^{-1}; **HRMS** calcd *m/z* for $C_{20}H_{21}F$ [M^+]: 280.1622; found 280.1620.

(7) Preparation of 2-phenyl-4-(4-chlorophenyl)-2,3-octadiene (3ag, QAN-2-159, cfsy-3-181)

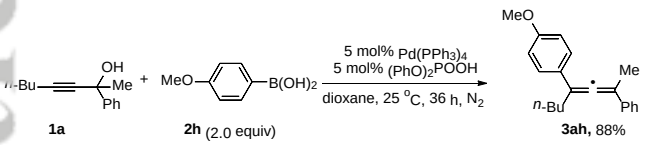


1a **2g** (2.0 equiv) **3ag**, 80%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.9 mg, 0.05 mmol), (4-chlorophenyl)boronic acid (312.7 mg, 2.0 mmol), $(PhO)_2POOH$ (12.6 mg, 0.05 mmol), **1a** (201.3 mg, 1.0 mmol), and

anhydrous dioxane (5 mL) at 25 °C afforded **3ag** (259.5 mg, 80%, 91% purity) as an oil [eluent: petroleum ether (200 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.42 (d, *J* = 7.2 Hz, 2 H, Ar-H), 7.37-7.26 (m, 4 H, Ar-H), 7.25-7.13 (m, 3 H, Ar-H), 2.59-2.42 (m, 2 H, CH_2), 2.20 (s, 3 H, CH_3), 1.59-1.48 (m, 2 H, CH_2), 1.47-1.33 (m, 2 H, CH_2), 0.90 (t, *J* = 7.4 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 205.5, 136.9, 135.5, 132.3, 128.5, 128.4, 127.3, 126.8, 125.6, 107.0, 104.0, 30.0, 29.9, 22.6, 16.8, 14.0; **MS** (70 eV, EI) *m/z* (%): 298 (M^+(^{37}Cl), 3.15), 296 (M^+(^{35}Cl), 9.08), 239 (100); **IR** (neat): *v* = 3056, 3025, 2959, 2924, 2857, 1929, 1594, 1489, 1462, 1405, 1181, 1090, 1067 cm^{-1}; **HRMS** calcd for $C_{20}H_{22}{}^{35}Cl$ [M+H$^+$]: 297.1405; found 297.1403.

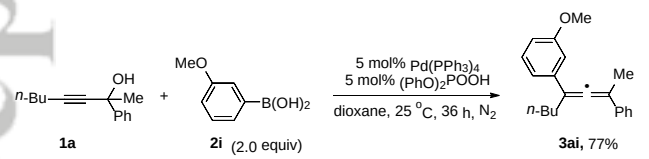
(8) Preparation of 2-phenyl-4-(4-methoxylphenyl)-2,3-octadiene (3ah, QAN-2-152)



1a **2h** (2.0 equiv) **3ah,** 88%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.9 mg, 0.05 mmol), (4-methoxyphenyl)boronic acid (304.1 mg, 2.0 mmol), $(PhO)_2POOH$ (12.6 mg, 0.05 mmol), **1a** (201.8 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3ah** (269.4 mg, 88%, 95% purity) as an oil [eluent: petroleum ether (150 mL) to petroleum ether/DCM/Et_2O = 200/1/1 (400 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.50-7.41 (m, 2 H, Ar-H), 7.38-7.25 (m, 4 H, Ar-H), 7.24-7.16 (m, 1 H, Ar-H), 6.85 (d, *J* = 8.4 Hz, 2 H, Ar-H), 3.79 (s, 3 H, CH_3), 2.65-2.42 (m, 2 H, CH_2), 2.19 (s, 3 H, CH_3), 1.60-1.50 (m, 2 H, CH_2), 1.48-1.33 (m, 2 H, CH_2), 0.90 (t, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 205.0, 158.5, 137.5, 129.2, 128.3, 127.1, 126.5, 125.6, 113.9, 107.3, 103.4, 55.3, 30.12, 30.08, 22.6, 16.9, 14.0; **MS** (70 eV, EI) *m/z* (%): 293 (M^++1, 4.92), 292 (M^+, 21.34), 235 (100); **IR** (neat): *v* = 3082, 3059, 2929, 2836, 1926, 1604, 1508, 1441, 1374, 1176, 1114, 1064 cm^{-1}; **HRMS** calcd for $C_{21}H_{25}O$ [M+H$^+$]: 293.1900; found 293.1897.

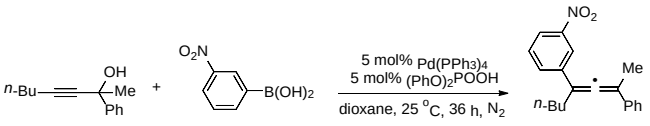
(9) Preparation of 2-phenyl-4-(3-methoxylphenyl)-2,3-octadiene (3ai, QAN-2-161)



1a **2i** (2.0 equiv) **3ai,** 77%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.7 mg, 0.05 mmol), (3-methoxyphenyl)boronic acid (304.1, 2.0 mmol), $(PhO)_2POOH$ (12.7 mg, 0.05 mmol), **1a** (201.8 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3ai** (231.8 mg, 77%, 97% purity) as an oil [eluent: petroleum ether (400 mL); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.44 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.31 (t, *J* = 7.8 Hz, 2 H, Ar-H), 7.27-7.12 (m, 2 H, Ar-H), 7.03 (d, *J* = 7.6 Hz, 1 H, Ar-H), 7.00-6.96 (m, 1 H, Ar-H), 6.75 (dd, J_1= 8.2 Hz, J_2= 2.2 Hz, 1 H, Ar-H), 3.78 (s, 3 H, CH_3), 2.62-2.42 (m, 2 H, CH_2), 2.20 (s, 3 H, CH_3), 1.64-1.50 (m, 2 H, CH_2), 1.46-1.33 (m, 2 H, CH_2), 0.90 (t, *J* = 7.4 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 205.6, 159.7, 138.7, 137.2, 129.3, 128.4, 126.6, 125.6, 118.7, 112.1, 111.7, 107.7, 103.6, 55.2, 30.1, 30.0, 22.6, 16.8, 14.0; **MS** (70 eV, EI) *m/z* (%): 293 (M^++1, 5.98), 292 (M^+, 25.45), 235 (100); **IR** (neat): *v* = 3059, 2957, 2929, 2836, 1925, 1604, 1580, 1440, 1374, 1240, 1176, 1114, 1040 cm^{-1}; **HRMS** calcd *m/z* for $C_{21}H_{24}O$ [M$^+$]: 292.1822; found 292.1827.

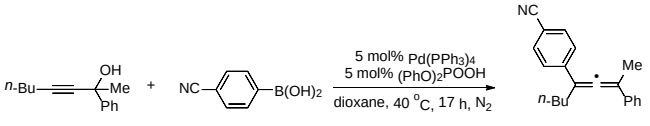
(10) Preparation of 2-phenyl-4-(3-nitrophenyl)-2,3-octadiene (3aj, QAN-2-150)



1a **2j** (2.0 equiv) **3aj,** 72%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.9 mg, 0.05 mmol), (3-nitrophenyl)boronic acid (334.0 mg, 2.0 mmol), $(PhO)_2POOH$ (12.7 mg, 0.05 mmol), **1a** (202.5 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3aj** (242.2 mg, 72%, 91% purity) as an oil [eluent: petroleum ether (150 mL) to petroleum ether/DCM/Et_2O = 100/1/1 (~400 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 8.23 (s, 1 H, Ar-H), 8.02 (d, *J* = 8.0 Hz, 1 H, Ar-H), 7.73 (d, *J* = 8.0 Hz, 1 H, Ar-H), 7.42 (t, *J* = 7.4 Hz, 3 H, Ar-H), 7.33 (t, *J* = 7.4 Hz, 2 H, Ar-H), 7.23 (t, *J* = 6.4 Hz, 2 H, Ar-H), 2.70-2.47 (m, 2 H, CH_2), 2.25 (s, 3 H, CH_3), 1.58 (quintet, *J* = 7.2 Hz, 2 H, CH_2), 1.50-1.33 (m, 2 H, CH_2), 0.93 (t, *J* = 7.4 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 205.9, 148.6, 139.3, 136.2, 132.2, 129.1, 128.5, 127.1, 125.7, 121.4, 120.3, 106.5, 105.1, 29.83, 29.80, 22.5, 16.7, 13.9; **MS** (70 eV, EI) *m/z* (%): 308 (M^++1, 2.72), 307 (M^+, 11.84), 250 (100); **IR** (neat): *v* = 3084, 2956, 2926, 2861, 1933, 1598, 1493, 1443, 1344, 1067, 1025 cm^{-1}; **HRMS** calcd for $C_{20}H_{21}NO_2$ [M$^+$]: 307.1572; found 307.1574.

(11) Preparation of 2-phenyl-4-(4-cyanophenyl)-2,3-octadiene (3ak, QAN-3-031)

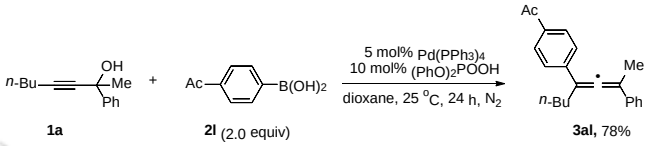


1a **2k** (2.0 equiv) **3ak,** 74%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.6 mg, 0.05 mmol), (4-cyanophenyl)boronic acid (294.0, 2.0 mmol), $(PhO)_2POOH$ (12.8 mg, 0.05 mmol), **1a** (202.0 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 40 °C afforded **3ak** (212.7 mg, 74%) as an oil eluent: petroleum ether (200 mL) to petroleum ether/DCM/Et_2O = 100/1/1 (400 mL) to petroleum ether/DCM/Et_2O = 50/1/1 (300 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.57 (d, *J* = 8.8 Hz, 2 H, Ar-H), 7.49 (d, *J* = 8.8 Hz, 2 H, Ar-H), 7.44-7.37 (m, 2 H, Ar-H), 7.34 (t, *J* = 7.6 Hz, 2 H, Ar-H), 727-7.21 (m, 1 H, Ar-H), 2.60-2.45 (m, 2 H, CH_2), 2.22 (s, 3 H, CH_3), 1.63-1.50 (m, 2 H, CH_2), 1.48-1.36 (m, 2 H, CH_2), 0.92 (t, *J* = 7.4 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 206.8, 142.2, 136.1, 132.2, 128.5, 127.1, 126.5, 125.6, 119.1, 109.8, 107.1, 104.8, 29.9, 29.6, 22.5, 16.6, 13.9; **MS** (70 eV, EI) *m/z* (%): 288 (M^++1, 1.12), 287 (M^+, 4.60), 230 (100); **IR** (neat): *v* = 3058, 2924, 2851, 2226, 1926, 1598, 1496, 1308, 1182, 1064, 1024 cm^{-1}; **HRMS** calcd *m/z* for $C_{21}H_{21}N$

[M⁺]: 287.1669; found 287.1661.

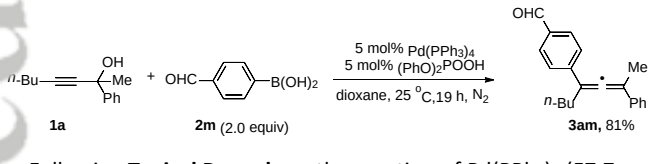
(12) Preparation of 2-phenyl-4-(4-acetylphenyl)-2,3-octadiene (3al, QAN-3-039)



1a **2l** (2.0 equiv) **3al,** 78%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), (4-acetylphenyl)boronic acid (327.8 mg, 2.0 mmol), $(PhO)_2POOH$ (25.2 mg, 0.10 mmol), **1a** (202.1 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3al** (237.0 mg, 78%) as an oil [eluent: petroleum ether/DCM/Et_2O = 100/1/1 (200 mL) to petroleum ether/DCM/Et_2O = 40/1/1 (~400 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.50 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.43 (d, *J* = 7.6 Hz, 2 H, Ar-H), 7.33 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.27-7.18 (m, 1 H, Ar-H), 2.62-2.46 (m, 5 H, CH_2 and CH_3), 2.23 (s, 3 H, CH_3), 1.57 (quintet, *J* = 7.3 Hz, 2 H, CH_2), 1.49-1.35 (m, 2 H, CH_2), 0.92 (t, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 206.8, 197.5, 142.2, 136.5, 135.3, 128.55, 128.46, 126.9, 126.0, 125.7, 107.5, 104.3, 30.0, 29.8, 26.5, 22.5, 16.7, 13.9; **MS** (70 eV, EI) *m/z* (%): 305 (M^++1, 6.24), 304 (M^+, 26.17), 43 (100); **IR** (neat): *v* = 3346, 3081, 2958, 2924, 2858, 1926, 1680, 1596, 1492, 1410, 1358, 1260, 1183, 1021 cm^{-1}; **HRMS** calcd for $C_{22}H_{24}O$ [M^+]: 304.1827; found 304.1831.

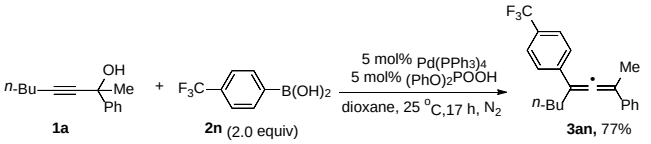
(13) Preparation of 2-phenyl-4-(4-formylphenyl)-2,3-octadiene (3am, QAN-3-122)



1a **2m** (2.0 equiv) **3am,** 81%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.7 mg, 0.05 mmol), (4-formylphenyl)boronic acid (300.1 mg, 2.0 mmol), $(PhO)_2POOH$ (12.7 mg, 0.05 mmol), **1a** (202.3 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3am** (236.4 mg, 81%) as a white solid [eluent: petroleum ether (200 mL) to petroleum ether/DCM/Et_2O = 50/1/1 (~410 mL)]; M.p. 56.3-59.4 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 9.96 (s, 1 H, CHO), 7.81 (d, *J* = 8.0 Hz, 2 H, Ar-H), 7.57 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.45-7.39 (m, 2 H, Ar-H), 7.34 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.26-7.20 (m, 1 H, Ar-H), 2.60-2.54 (m, 2 H, CH_2), 2.24 (s, 3 H, CH_3), 1.63-1.50 (m, 2 H, CH_2), 1.49-1.39 (m, 2 H, CH_2), 0.92 (t, *J* = 7.4 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 207.2, 191.7, 143.8, 136.4, 134.7, 129.9, 128.5, 127.0, 126.4, 125.7, 107.6, 104.5, 30.0, 29.8, 22.5, 16.7, 13.9; **MS** (70 eV, EI) *m/z* (%): 291 (M^++1, 3.75), 290 (M^+, 15.17), 205 (100); **IR** (neat): *v* = 3356, 3083, 2925, 2854, 1924, 1694, 1596, 1491, 1459, 1304, 1208, 1110, 1064 cm^{-1}; Anal. Calcd. for $C_{21}H_{22}O$(%): C: 86.85, H: 7.64; Found: C: 86.66, H: 7.69.

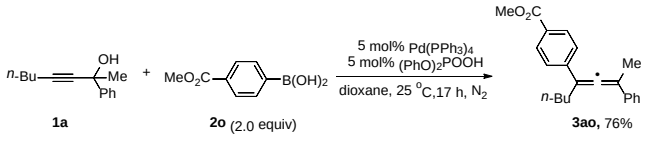
(14) Preparation of 2-phenyl-4-(4-trifluoromethylphenyl)-2,3-octadiene (3an, QAN-2-157)



1a **2n** (2.0 equiv) **3an,** 77%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), (4-(trifluoromethyl)phenyl)boronic acid (378.0 mg, 2.0 mmol), $(PhO)_2POOH$ (12.6 mg, 0.05 mmol), **1a** (202.5 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3an** (282.0 mg, 77%, 91% purity) as an oil [eluent: petroleum ether (200 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.59-7.45 (m, 4 H, Ar-H), 7.43 (d, *J* = 7.6 Hz, 2 H, Ar-H), 7.33 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.23 (t, *J* = 7.2 Hz, 1 H, Ar-H), 2.63-2.44 (m, 2 H, CH_2), 2.22 (s, 3 H, CH_3), 1.63-1.51 (m, 2 H, CH_2), 1.49-1.33 (m, 2 H, CH_2), 0.92 (t, *J* = 7.2 Hz, 3 H, CH_3); **^{19}F NMR** (376 MHz, $CDCl_3$): δ = -62.9; **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 206.3, 140.9, 136.6, 128.54 (q, *J* = 32.1 Hz), 128.51, 127.0, 126.2, 125.7, 125.3 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 270.2 Hz), 107.1, 104.4, 30.0, 29.8, 22.6, 16.7, 13.9; **MS** (70 eV, EI) *m/z* (%): 331 (M^++1, 2.52), 330 (M^+, 10.68), 273 (100); **IR** (neat): *v* = 3082, 2957, 2933, 2866, 1927, 1613, 1463, 1375, 1323, 1156, 1113, 1066 cm^{-1}; **HRMS** calcd for $C_{21}H_{21}F_3$ [M^+]: 330.1595; found 330.1597.

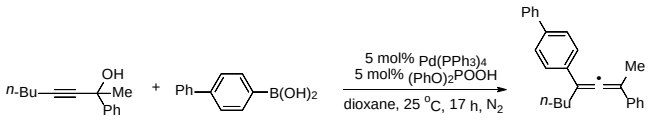
(15) Preparation of 2-phenyl-4-(4-methoxylcarbonylphenyl)-2,3-octadiene (3ao, QAN-2-145)



1a **2o** (2.0 equiv) **3ao,** 76%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), (4-(methoxycarbonyl)phenyl)boronic acid (360.1 mg, 2.0 mmol), $(PhO)_2POOH$ (12.6 mg, 0.05 mmol), **1a** (202.1 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3ao** (246.1 mg, 76%, 99% purity) as a white solid [eluent: petroleum ether (200 mL) to petroleum ether/DCM/Et_2O = 100/1/1 (200 mL)]; M.p. 65.7-70.8 °C (petroleum ether/dichloromethane); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.52-7.38 (m, 4 H, Ar-H), 7.33 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.22-7.16 (m, 1 H, Ar-H), 3.90 (s, 3 H, CH_3), 2.63-2.50 (m, 2 H, CH_2), 2.22 (s, 3 H, CH_3), 1.62-1.43 (m, 2 H, CH_2), 1.50-1.32 (m, 2 H, CH_2), 0.91 (t, *J* = 7.4 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 206.6, 166.9, 142.0, 136.6, 129.7, 128.4, 128.1, 126.9, 125.8, 125.6, 107.5, 104.2, 52.0, 30.0, 29.8, 22.5, 16.7, 13.9; **MS** (70 eV, EI) *m/z* (%):321 (M^++1, 3.04), 320 (M^+, 12.24), 263 (100); **IR** (neat): *v* = 3033, 2954, 2923, 2860, 1928, 1712, 1602, 1494, 1372, 1271, 1180, 1106, 1019 cm^{-1}; Anal. Calcd. for $C_{22}H_{24}O_2$(%): C: 82.46, H: 7.55; Found: C: 82.37, H: 7.62.

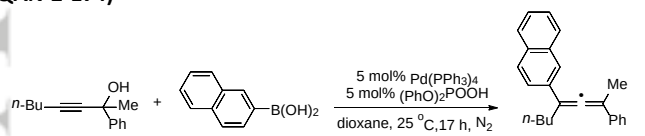
(16) Preparation of 2-phenyl-4-biphenyl-2,3-octadiene (3ap, QAN-2-169)



1a **2p** (2.0 equiv) **3ap,** 82%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.7 mg, 0.05 mmol), [1,1'-biphenyl]-4-ylboronic acid (396.3, 2.0 mmol), $(PhO)_2POOH$ (12.6 mg, 0.05 mmol), **1a** (202.3 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3ap** (302.6 mg, 82%, purity: 92%) as an oil [eluent: petroleum ether (200 mL); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.63-7.38 (m, 10 H, Ar-H), 7.36-7.27 (m, 3 H, Ar-H), 7.25-7.16 (m, 1 H, Ar-H), 2.58 (t, *J* = 7.4 Hz, 2 H, CH_2), 2.23 (s, 3 H, CH_3), 1.59 (quintet, *J* = 7.5 Hz, 2 H, CH_2), 1.50-1.35 (m, 2 H, CH_2), 0.92 (t, *J* = 7.4 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 205.8, 140.9, 139.5, 137.2, 136.0, 128.7, 128.4, 127.1, 126.9, 126.7, 126.5, 125.7, 107.5, 103.8, 30.1, 30.0, 22.6, 16.9, 14.0; **MS** (70 eV, EI) *m/z* (%): 339 (M^++1, 6.58), 338 (M^+, 22.32), 281 (100); **IR** (neat): *v* = 3055, 3027, 2923, 2857, 1931, 1596, 1486, 1370, 1230, 1111, 1067 cm^{-1}; **HRMS** calcd *m/z* for $C_{26}H_{26}$ [M^+]: 338.2029; found 338.2027.

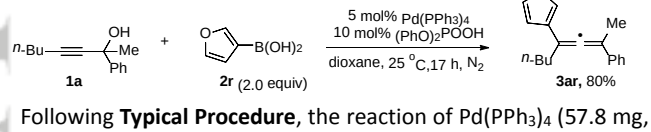
(17) Preparation of 2-phenyl-4-(2-napthyl)-2,3-octadiene (3aq, QAN-2-174)



1a **2q** (2.0 equiv) **3aq,** 88%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), naphthalen-2-ylboronic acid (344.2 mg, 2.0 mmol), $(PhO)_2POOH$ (12.6 mg, 0.05 mmol), **1a** (202.6 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3aq** (276.0 mg, 88%) as a white solid [eluent: petroleum ether (200 mL)]; M.p. 72.7-79.8 °C; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.87-7.43 (m, 3 H, Ar-H), 7.71 (d, *J* = 8.8 Hz, 1 H, Ar-H), 7.63-7.52(m, 1 H, Ar-H), 7.50-7.36 (m, 4 H, Ar-H), 7.33 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.28-7.15 (m, 1 H, Ar-H), 2.68 (t, *J* = 7.6 Hz, 2 H, CH_2), 2.25 (s, 3 H, CH_3), 1.63 (quintet, *J* = 7.5 Hz, 2 H, CH_2), 1.53-1.37 (m, 2 H, CH_2), 0.93 (t, *J* = 7.4 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 206.3, 137.2, 136.5, 133.7, 132.5, 128.4, 128.0, 127.8, 127.5, 126.7, 126.0, 125.7, 125.6, 125.5, 123.6, 108.1, 103.9, 30.1, 30.0, 22.7, 16.9, 14.0; **MS** (70 eV, EI) *m/z* (%): 313 (M^++1, 5.92), 312 (M^+, 22.68), 255 (100); **IR** (neat): *v* = 3055, 2955, 2923, 2866, 1922, 1628, 1595, 1491, 1463, 1261, 1187, 1127, 1064 cm^{-1}; **HRMS** calcd *m/z* for $C_{24}H_{24}$ [M^+]: 312.1873; found 312.1870.

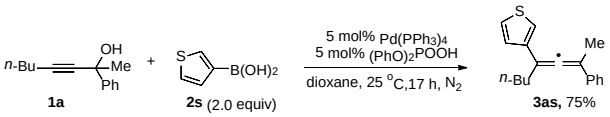
(18) Preparation of 2-phenyl-4-(3-furyl)-2,3-octadiene (3ar, QAN-3-003)



1a **2r** (2.0 equiv) **3ar,** 80%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), furan-3-ylboronic acid (223.9 mg, 2.0 mmol), $(PhO)_2POOH$ (25.2 mg, 0.10 mmol), **1a** (202.4 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3ar** (201.8 mg, 80%) as an oil [eluent: petroleum ether (300 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.48-7.37 (m, 3 H, Ar-H), 7.36-7.26 (m, 3 H, Ar-H), 7.20 (t, *J* = 7.4 Hz, 1 H, Ar-H), 6.35 (d, *J* = 0.8 Hz, 1 H, Ar-H), 2.48-2.25 (m, 2 H, CH_2), 2.17 (s, 3 H, CH_3), 1.62-1.50 (m, 2 H, CH_2), 1.48-1.31 (m, 2 H, CH_2), 0.90 (t, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 204.1, 143.1, 138.2, 137.4, 128.3, 126.6, 125.8, 123.5, 109.4, 103.2, 100.6, 30.7, 29.9, 22.6, 17.0, 14.0; **MS** (70 eV, EI) *m/z* (%): 253 (M^++1, 4.92), 252 (M^+, 15.16), 105 (100); **IR** (neat): *v* = 3059, 2956, 2927, 2863, 1935, 1762, 1598, 1446, 1265, 1157, 1066 cm^{-1}; **HRMS** calcd for $C_{18}H_{20}O$ [M^+]: 252.1514; found 252.1510.

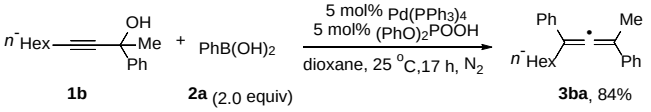
(19) Preparation of 2-phenyl-4-(3-thienyl)-2,3-octadiene (3as, QAN-2-196)



1a **2s** (2.0 equiv) **3as,** 75%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), thiophen-3-ylboronic acid (256.1mg, 2.0 mmol), $(PhO)_2POOH$ (12.6 mg, 0.05 mmol), **1a** (201.9 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3as** (217.1 mg, 75%, 93% purity) as an oil [eluent: petroleum ether (300 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.48-7.38 (m, 2 H, Ar-H), 7.34-7.25 (m, 2 H, Ar-H), 7.23-7.15 (m, 2 H, Ar-H), 7.14-7.03 (m, 2 H, Ar-H), 2.32 (dt, J_1 = 7.2 Hz, J_2 = 2.3 Hz, 2 H, CH_2), 2.18 (s, 3 H, CH_3), 1.57 (quintet, *J* = 7.4 Hz, 2 H, CH_2), 1.48-1.33 (m, 2 H, CH_2), 0.90 (t, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 205.3, 139.0, 137.3, 128.3, 127.0, 126.6, 125.7, 125.2, 118.8, 104.1, 103.2, 30.7, 30.0, 22.6, 17.0, 14.0; **MS** (70 eV, EI) *m/z* (%): 269 (M^++1, 5.23), 268 (M^+, 24.95), 211 (100); **IR** (neat): *v* = 3026, 2954, 2924, 2858, 1934, 1597, 1491, 1373, 1233, 1178, 1065 cm^{-1}; **HRMS** calcd for $C_{18}H_{20}S$ [M^+]: 268.1286; found 268.1289.

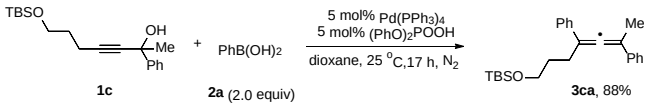
(20) Preparation of 2,4-diphenyl-2,3-decadiene (3ba, QAN-3-090)



1b **2a** (2.0 equiv) **3ba**, 84%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), phenylboronic acid (243.9, 2.0 mmol), $(PhO)_2POOH$ (12.6 mg, 0.05 mmol), **1b** (229.8 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3ba** (251.1 mg, 84%, 96% purity) as an oil [eluent: petroleum ether (200 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.43 (t, *J* = 7.4 Hz, 4 H, Ar-H), 7.34-7.26 (m, 4 H, Ar-H), 7.22-7.15 (m, 2 H, Ar-H), 2.60-2.45 (m, 2 H, CH_2), 2.20 (s, 3 H, CH_3), 1.58 (quintet, *J* = 7.4 Hz, 2 H, CH_2), 1.45-1.32 (m, 2 H, CH_2), 1.29-1.20 (m, 4 H, 2 x CH_2), 0.85 (t, *J* = 6.6 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, CDCl3): δ = 205.6, 137.3, 137.1 128.40, 128.37, 126.7, 126.6, 126.1, 125.6, 107.8, 103.6, 31.7, 30.2, 29.3, 27.9, 22.7, 16.8, 14.0; **MS** (70 eV, EI) *m/z* (%): 291 (M^++1, 1.68), 290 (M^+, 6.86), 205 (100); **IR** (neat): *v* = 3027, 2923, 2855, 1935, 1595, 1490, 1447, 1372, 1181, 1067, 1024 cm^{-1}; **HRMS** calcd for $C_{22}H_{26}$ [M^+]: 290.2035; found 290.2037.

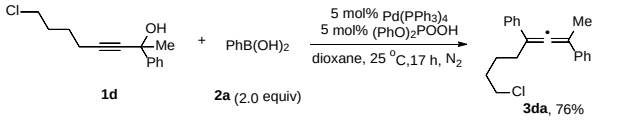
(21) Preparation of 2,4-diphenyl-2,3-heptadiene-7-(*tert*-butyldimethylsilyloxy) ether (3ca, QAN-3-102)



1c **2a** (2.0 equiv) **3ca**, 88%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), phenylboronic acid (244.2 mg, 2.0 mmol), $(PhO)_2POOH$ (12.6 mg, 0.05 mmol), **1c** (318.3 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3ca** (332.9 mg, 88%) as an oil [eluent: petroleum ether (200 mL) to petroleum ether/DCM/Et_2O = 100/1/1 (400 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.49-7.43 (m, 4 H, Ar-H), 7.35-7.28 (m, 4 H, Ar-H), 7.24-7.17 (m, 2 H, Ar-H), 3.72 (t, *J* = 6.2 Hz, 2 H, CH_2), 2.65 (t, *J* = 7.4 Hz, 2 H, CH_2), 2.22 (s, 3 H, CH_3), 1.90-1.79 (m, 2 H, CH_2), 0.91 (s, 9 H, 3 x CH_3), 0.05 (s, 6 H, 2 x CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 205.4, 137.1, 136.9, 128.42, 128.39, 126.73, 126.69, 126.0, 125.6, 107.5, 104.0, 62.8, 31.2, 26.5, 26.0, 18.3, 16.9, -5.3; **MS** (ESI) *m/z* (%): 247 ([M-OTBS)$^+$, 379 (M+H)$^+$; **IR** (neat): *v* = 3056, 3028, 2930, 2856, 1933, 1935, 1596, 1491, 1460, 1384, 1251, 1184, 1098 cm^{-1}; **HRMS** calcd for $C_{25}H_{35}OSi$ [M+H] $^+$: 379.2452; found 379.2448.

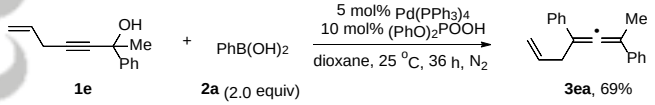
(22) Preparation of 2,4-diphenyl-8-chloro-2,3- octadien (3da, QAN-3-103)



1d **2a** (2.0 equiv) **3da**, 76%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), phenylboronic acid (244.2 mg, 2.0 mmol), $(PhO)_2POOH$ (12.6 mg, 0.05 mmol), **1d** (236.5 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3da** (234.8 mg, 76%, 96% purity) as an oil [eluent: petroleum ether (500 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.49-7.38 (m, 4 H, Ar-H), 7.36-7.21 (m, 4 H, Ar-H), 7.25-7.15 (m, 2 H, Ar-H), 3.50 (t, *J* = 6.8 Hz, 2 H, CH_2), 2.58 (t, *J* = 7.6 Hz, 2 H, CH_2), 2.21 (s, 3 H, CH_3), 1.92-1.81 (m, 2 H, CH_2), 1.78-1.62 (m, 2 H, CH_2); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 205.4, 136.9, 136.6, 128.5, 128.4, 126.81, 126.77, 126.0, 125.6, 107.1, 104.1, 44.7, 32.3, 29.4, 25.1, 16.9; **MS** (70 eV, EI) *m/z* (%): 298 ([M(^{35}Cl), 3.17), 296 (M$^+$(^{35}Cl), 8.77), 205 (100); **IR** (neat): *v* = 3078, 2988, 2941, 2853, 1927, 1591, 1444, 1331, 1283, 1209, 1069 cm^{-1}; **HRMS** calcd for $C_{20}H_{22}{}^{35}Cl$ [M+H $^+$]: 297.1405; found 297.1403.

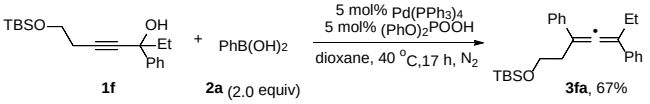
(23) Preparation of 2,4-diphenyl-2,3,6-heptatriene (3ea, QAN-3-107)



1e **2a** (2.0 equiv) **3ea**, 69%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.9 mg, 0.05 mmol), phenylboronic acid (244.0 mg, 2.0 mmol), $(PhO)_2POOH$ (25.0 mg, 0.10 mmol), **1e** (185.9 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3ae** (170.0 mg, 69%) as an oil [eluent: petroleum ether (400 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.46-7.40 (m, 4 H, Ar-H), 7.34-7.28 (m, 4 H, Ar-H), 7.22-7.17 (m, 2 H, Ar-H), 6.05-5.90 (m, 1 H, =CH), 5.22-5.14 (m, 1 H, =CH), 5.08-5.01 (m, 1 H, =CH), 3.28-3.34 (m, 2 H, CH_2), 2.20 (s, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 206.0, 137.0, 136.4, 135.8, 128.42, 128.39, 126.8, 126.1, 125.7, 116.2, 106.1, 104.0, 34.9, 16.8; **MS** (70 eV, EI) *m/z* (%): 247 (M$^+$+1, 12.63), 246 (M$^+$, 59.29), 154 (100); **IR** (neat): *v* = 3063, 2913, 1941, 1590, 1472, 1438, 1379, 1174, 1079 cm^{-1}; **HRMS** calcd for $C_{19}H_{18}$ [M$^+$]: 246.1409; found 246.1406.

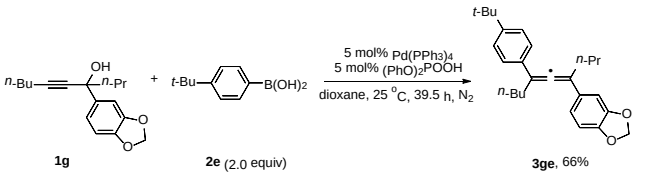
(24) Preparation of 3,5-diphenyl-3,4-heptadiene-7-(*tert*-butyldimethylsilyloxy) ether (3fa, QAN-3-058)



1f **2a** (2.0 equiv) **3fa**, 67%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), phenylboronic acid (243.7 mg, 2.0 mmol), $(PhO)_2POOH$ (12.7 mg, 0.05 mmol), **1f** (318.2 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 40 °C afforded **3fa** (257.4 mg, 67%, 98% purity) as an oil [eluent: petroleum ether (200 mL) to petroleum ether/DCM/Et_2O = 100/1/1 (200 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.64-7.51 (m, 4 H, Ar-H), 7.44 (t, *J* = 7.6 Hz, 4 H, Ar-H), 7.37-7.27 (m, 2 H, Ar-H), 4.10-3.90 (m, 2 H, CH_2), 2.96 (t, *J* = 7.4 Hz, 2 H, CH_2), 2.78-2.58 (m, 2 H, CH_2), 1.31 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.03-0.90 (m, 9 H, 3 x CH_3), 0.16 (d, *J* = 3.6 Hz, 6 H, 2 x CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 205.0, 136.7, 128.44, 128.42, 128.2, 126.8, 125.9, 125.8, 110.8, 106.5, 62.3, 33.8, 25.94, 25.88, 23.3, 18.3, 12.6, -5.3; **MS** (70 eV, EI) *m/z* (%): 378 (M$^+$, 1.25), 349 (100); **IR** (neat): *v* = 3029, 2955, 2930, 2857, 1934, 1595, 1491, 1460, 1387, 1252, 1096 cm^{-1}; **HRMS** calcd for $C_{25}H_{34}OSi$ [M$^+$]: 378.2379; found 378.2385.

(25) Preparation of 4-(3,4-methylenedioxyphenyl)-6-(4-*t*-butylphenyl)-4,5-decadiene (3ge, QAN-3-046)

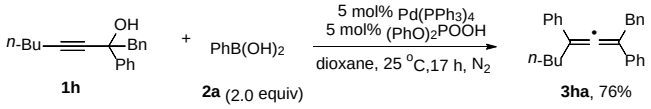


1g **2e** (2.0 equiv) **3ge**, 66%

Following **Typical Procedure,** the reaction of $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), (4-(tert-butyl)phenyl)boronic acid (356.3 mg, 2.0 mmol), $(PhO)_2POOH$ (12.8 mg, 0.05 mmol), **1g** (274.0 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3ge** (257.4 mg, 66%) as a white solid [eluent: petroleum ether (200 mL) to petroleum ether/DCM/Et_2O = 100/1/1 (400 mL)]; M.p. 67.2-71.2 °C (petroleum ether/ethyl acetate); **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.45-7.28 (m, 4 H, Ar-H), 7.01-6.83 (m, 2 H, Ar-H), 6.75 (d, *J* = 8.0 Hz, 1 H, Ar-H), 5.98-5.82 (m, 2 H, CH_2), 2.59-2.37 (m, 4 H, 2 x CH_2), 1.62-1.52 (m, 4 H, 2 x CH_2), 1.46-1.35 (m, 2 H, CH_2), 1.31 (s, 9 H, 3 x CH_3), 0.99 (t, *J* = 7.2 Hz, 3 H, CH_3), 0.91 (t, *J* = 7.4 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 204.7, 149.6, 147.8, 146.4, 134.1, 131.4, 125.5, 125.3, 118.9, 108.8, 108.7, 108.1, 106.7, 100.9, 34.4, 32.9, 31.3, 30.3, 30.1, 22.8, 21.4, 14.3, 14.0; MS (ESI) m/z: 391 ([M+H$^+$]); **IR** (neat): *v* = 3080, 2956, 2927, 2871, 1926,

1602, 1503, 1464, 1362, 1111, 1086, 1042 cm^{-1}; Anal. Calcd. for $C_{27}H_{34}O_2$ (%): C: 83.03, H: 8.77; Found: C: 82.60, H: 8.78

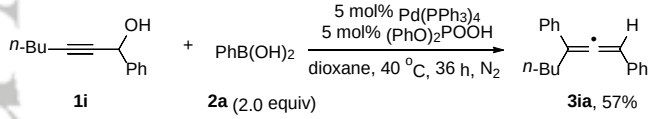
(26) Preparation of 1,3-diphenyl-1-benzyl-2,3-heptadiene (3ha, QAN-3-106)



1h **2a** (2.0 equiv) **3ha**, 76%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), phenylboronic acid (244.1 mg, 2.0 mmol), $(PhO)_2POOH$ (12.7 mg, 0.05 mmol), **1h** (278.9 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 25 °C afforded **3ha** (257.1 mg, 76%) as an oil [eluent: petroleum ether (600 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.47-7.41 (m, 2 H, Ar-H), 7.35-7.24 (m, 2 H, Ar-H), 7.30-7.23 (m, 6 H, Ar-H), 7.22-7.10 (m, 5 H, Ar-H), 3.90 (s, 2 H, CH_2), 2.58-2.38 (m, 2 H, CH_2), 1.51-1.41 (m, 2 H, CH_3), 1.40-1.30 (m, 2 H, CH_2), 0.87 (t, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 206.8, 139.4, 136.7, 136.5, 128.9, 128.4, 128.3, 128.2, 126.73, 126.69, 126.11, 126.06, 126.04, 109.4, 107.9, 37.2, 30.21, 30.18, 22.7, 14.0; **MS** (70 eV, EI) *m/z* (%): 339 (M^++1, 4.70), 338 (M^+, 17.22), 91 (100); **IR** (neat): *v* = 3039, 2935, 2859, 1941, 1591, 1468, 1444, 1375, 1173, 1018 cm^{-1}; **HRMS** calcd for $C_{26}H_{26}$ [M^+]: 338.2035; found 338.2038.

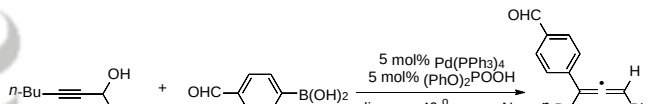
(27) Preparation of 1,3-diphenyl-1,2-heptadiene (3ia, QAN-3-151)



1i **2a** (2.0 equiv) **3ia**, 57%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.9 mg, 0.05 mmol), phenylboronic acid (243.8 mg, 2.0 mmol), $(PhO)_2POOH$ (12.5 mg, 0.05 mmol), **1i** (188.1mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 40 °C afforded **3ia**[6h] (142.1 mg, 57%) as an oil [eluent: petroleum ether (200 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 7.6 Hz, 2 H, Ar-H), 7.36-7.27 (m, 6 H, Ar-H), 7.23-7.16 (m, 2 H, Ar-H), 6.52 (t, *J* = 2.8 Hz, 1 H, =CH), 2.63-2.47 (m, 2 H, CH_2), 1.66-1.54 (m, 2 H, CH_2), 1.48-1.38 (m, 2 H, CH_2), 0.92 (t, *J* = 7.4 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 206.5, 136.3, 136.2, 128.7, 128.5, 127.0, 126.9, 126.7, 126.1, 110.0, 97.8, 30.1, 29.9, 22.6, 13.9`; **MS** (70 eV, EI) *m/z* (%): 248 (M^+, 4.04), 105 (100); **IR** (neat): *v* = 3028, 2928, 2870, 1932, 1724, 1597, 1493, 1447, 1378, 1264, 1204, 1071 cm^{-1}.

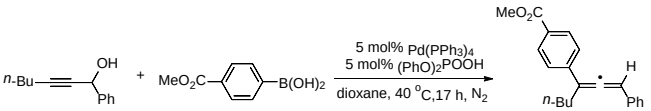
(28) Preparation of 1-phenyl-3-(4-formylphenyl)-1,2-heptadiene (3im, QAN-3-155)



1i **2m** (2.0 equiv) **3im**, 63%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.7 mg, 0.05 mmol), (4-formylphenyl)boronic acid (299.7 mg, 2.0 mmol), $(PhO)_2POOH$ (12.6 mg, 0.05 mmol), **1i** (188.0 mg, 1.0 mmol), and anhydrous dioxane (5 mL) of 40 °C afforded **3im** (173.6 mg, 63%) as an oil [eluent: petroleum ether/DCM/Et_2O = 100/1/1 (200 mL) to petroleum ether/DCM/Et_2O = 50/1/1 (400 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 9.98 (s, 1 H, CHO), 7.82 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.60 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.36-7.28 (m, 4 H, Ar-H), 7.23-7.16 (m, 1 H, Ar-H), 6.60 (t, *J* = 3.0 Hz, 1 H, =CH), 2.62-2.52 (m, 2 H, CH_2), 1.68-1.56 (m, 2 H, CH_2), 1.48-1.40 (m, 2 H, CH_2), 0.93 (t, *J* = 7.4 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 208.0, 191.7, 142.9, 135.0, 133.8, 129.9, 128.8, 127.4, 126.9, 126.6, 109.7, 98.5, 30.0, 29.7, 22.6, 13.9; **MS** (70 eV, EI) *m/z* (%): 276 (M^+, 1.33), 133 (100); **IR** (neat): *v* = 3030, 2957, 2930, 2869, 1930, 1697, 1600, 1454, 1383, 1169, 1013 cm^{-1}; **HRMS** calcd for *m/z* $C_{20}H_{20}O$ [M^+]: 276.1509; found 276.1513.

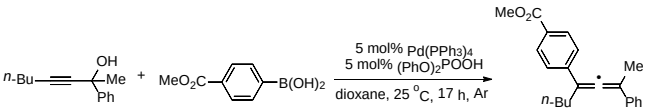
(29) Preparation of 1-phenyl-3-(4-methoxylcarbonylphenyl)-1,2-heptadiene (3io, QAN-3-148)



1i **2o** (2.0 equiv) **3io**, 74%

Following **Typical Procedure**, the reaction of $Pd(PPh_3)_4$ (57.8 mg, 0.05 mmol), (4-(methoxycarbonyl)phenyl)boronic acid (360.1 mg, 2.0 mmol), $(PhO)_2POOH$ (12.5 mg, 0.05 mmol), **1i** (188.3 mg, 1.0 mmol), and anhydrous dioxane (5 mL) at 40 °C afforded **3io**[6h] (226.7 mg, 74%) as an oil [eluent: petroleum ether/ethyl acetate = 60/1 (240 mL) to petroleum ether/ethyl acetate = 30/1 (300 mL) to petroleum ether/ethyl acetate = 20/1 (200 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.50 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.35-7.27 (m, 4 H, Ar-H), 7.24-7.18 (m, 1 H, Ar-H), 6.58 (t, *J* = 2.8 Hz, 1 H, =CH), 3.90 (s, 3 H, OCH_3), 2.62-2.47 (m, 2 H, CH_2), 1.64-1.53 (m, 2 H, CH_2), 1.48-1.39 (m, 2 H, CH_2), 0.92 (t, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 207.5, 166.9, 141.2, 134.0, 129.8, 128.8, 128.5, 127.2, 126.8, 126.0, 109.6, 98.3, 52.0, 30.0. 29.7, 22.6, 13.9; **MS** (70 eV, EI) *m/z* (%): 306 (M^+, 1.5), 163 (100); **IR** (neat): *v* = 3029, 2954, 2930, 2867, 1931, 1719, 1604, 1435, 1409, 1185, 1016 cm^{-1}.

2. Gram scale synthesis of 2-phenyl-4-(4-methoxylcarbonylphenyl)-2,3-octadiene (3ao, QAN-3-119)

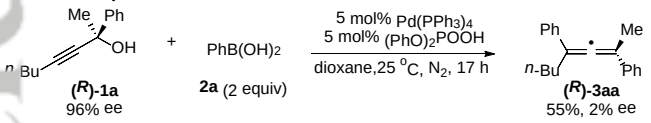


1a **2o** (2.0 equiv) **3ao**, 91%

To an oven-dried 100 mL Schlenk tube were added (4-(methoxycarbonyl)phenyl)boronic acid (1.7962 g, 10.0 mmol), $(PhO)_2POOH$ (62.6 mg, 0.25 mmol), and $Pd(PPh_3)_4$ (288.9 mg, 0.25 mmol). After replacing air with argon for three times at rt by vacuum, **1a** (1.0065 g, 5.0 mmol), and anhydrous dioxane (25 mL) were added sequentially. The reulting mixture was stirred for 17 h in oil bath at 25 °C and filtered through a short column of silica gel (3 cm) eluted with ethyl acetate (50 mL). After removal of the solvent under vacuum, the crude product was analyzed by ^{1}H NMR with CH_2Br_2 (70 μL) as the internal standard: 96% NMR yield of **3ao** was formed based on ^{1}H NMR analysis. The residue was

purified by column chromatography on silica gel to afford **3ao** (1.4572 g, 91%) as a white solid eluent: petroleum ether/DCM/Et_2O = 100/1/1 (~200 mL) to petroleum ether/DCM/Et_2O = 50/1/1 (~200 mL) to petroleum ether/DCM/Et_2O = 40/1/1 (420 mL)]; **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.96 (d, *J* = 8.4 Hz, 2 H, Ar-H), 7.50-7.40 (m, 4 H, Ar-H), 7.32 (t, *J* = 7.6 Hz, 2 H, Ar-H), 7.25-7.18 (m, 1 H, Ar-H), 3.89 (s, 3 H, CH_3), 2.58-2.51 (m, 2 H, CH_2), 2.22 (s, 3 H, CH_3), 1.63-1.51 (m, 2 H, CH_2), 1.48-1.35 (m, 2 H, CH_2), 0.91 (t, *J* = 7.2 Hz, 3 H, CH_3); **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 206.6, 167.0, 142.0, 136.6, 129.7, 128.4, 128.1, 126.9, 125.8, 125.7, 107.5, 104.2, 51.9, 30.0, 29.8, 22.5, 16.7, 13.9.

3. Preparation of (*R*)- 2,4-diphenyl-2,3-octadiene ((*R*)-3aa, OAN-3-125)



Following Typical Procedure **I**, The reaction of $Pd(PPh_3)_4$ (11.6 mg, 0.01 mmol), phenylboronic acid (49.0 mg, 0.4 mmol), $(PhO)_2POOH$ (2.5 mg, 0.01 mmol), **(*R*)-1a** (40.3 mg, 0.2 mmol), and anhydrous dioxane (1 mL) of 25 ℃ afforded **(*R*)-3aa** (28.7 mg, 55%, 2% ee) as an oil [eluent: petroleum ether (200 mL)]; HPLC conditions: OJ-H column, hexane/*i*-PrOH = 200/1, 0.7 mL/min, λ= 214 nm, t_R (minor) = 6.2 min, t_R (major) = 7.5 min.

4. Biological Activity Study

(1) GLP-1 measurement

Mouse intestinal cell line STC-1 was kindly provided by Dr. Jia Li (Shanghai Institute of Materia Medica, Chinese Academy of Sciences) and cultured in DMEM medium, containing 15% FBS, 100 U/mL penicillin and 100 μg/mL streptomycin at 37 °C in a humidified atmosphere of 5% CO_2. The cells were seeded in 96-well plates at a density of 40000 cells/well. After cultured overnight, the cells were treated 0.1% DPP-IV inhibitor PK44 in KRB buffer containing 0.2% fatty acid-free BSA for 2 hr. Cells were then treated with vehicle control (DMSO), positive control (1.0 μM PMA) or tested compounds for another 2 hr. The supernatants of the culture medium were collected and the concentration of GLP-1 in the supernatants was measured by using active GLP-1 kit according to the manufacturer's instructions (Cisbio, Bedford, MA).

(2) Glucose consumption

Rat L6 myotube cells were kindly provided by Dr. Jia Li (Shanghai Institute of Materia Medica, Chinese Academy of Sciences) and cultured in high-glucose (4.5 g/L) DMEM medium supplemented with 10% FBS, 100 U/mL penicillin and 100 μg/mL streptomycin. For differentiation, the cells were maintained in high-glucose (4.5 g/L) DMEM containing 2% FBS for 6 days and the medium was changed every two days. After differentiation, the myotube cells were incubated in serum-free, low-glucose (1.0 g/L) DMEM medium for 6 hr and treated with vehicle control (DMSO), positive control (10 mM metformin) or tested compounds for 24 hr. The concentration of glucose in medium was measured with glucose assay reagent (Mingdian, Shanghai, China) according to the glucose oxidase method.

Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.2018xxxxx.

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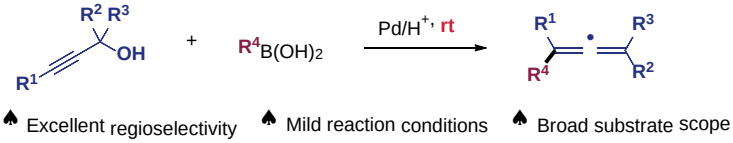

♠ Excellent regioselectivity ♠ Mild reaction conditions ♠ Broad substrate scope

Pd/H⁺ co-catalyzed cross-coupling of propargylic alcohols with boronic acids has been established for the synthesis of tri- and tetra-substituted allenes with various useful functional groups.

Yani Qin, Hui Qian, Qin Chen,* and Shengming Ma*

