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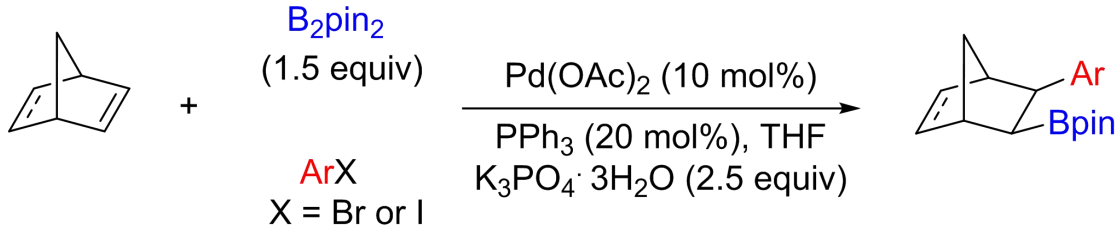
Palladium-Catalyzed Arylboration of Bicyclic Alkenes

Kai Yang[a] and Qiuling Song[a, b] *

[a] Institute of Next Generation Matter Transformation, College of Chemical Engineering at Huaqiao University, 668 Jimei Blvd, Xiamen, Fujian, 361021, P. R. China

[b] National Laboratory for Molecular Sciences, Institute of Chemistry, CAS, Beijing, 100190, P. R. China

Email: qsong@hqu.edu.cn

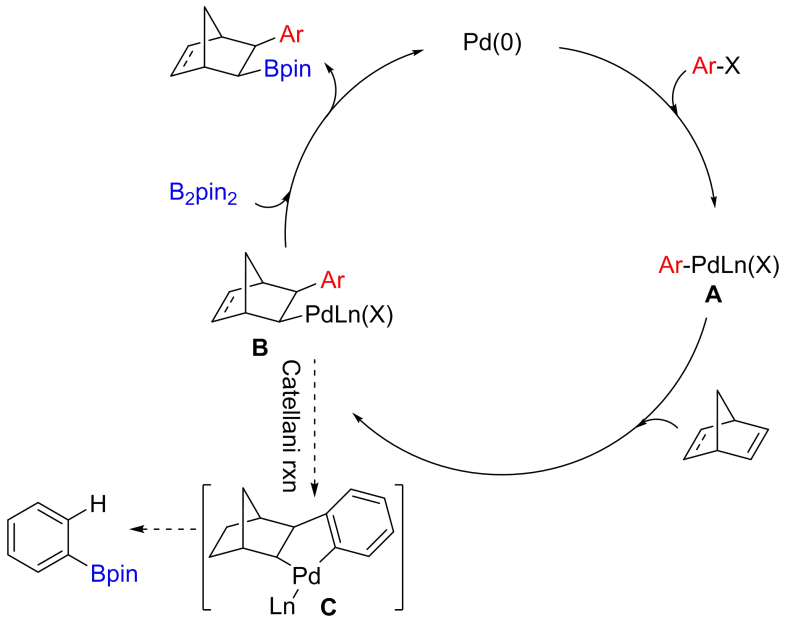


ABSTRACT: A palladium-catalyzed arylboration of norbornene or norbornadiene with aryl halides and bis(pinacolato)diboron has been disclosed. Mechanistic studies suggest that the reaction proceeds under a Catellani-type coupling to render versatile multi-functionalized alkylboranes in good yields. This reaction is complementary to the existing methods and is well tolerable with a variety of functional groups and readily scaled-up to a gram scale without deteriorating the yield.

INTRODUCTION

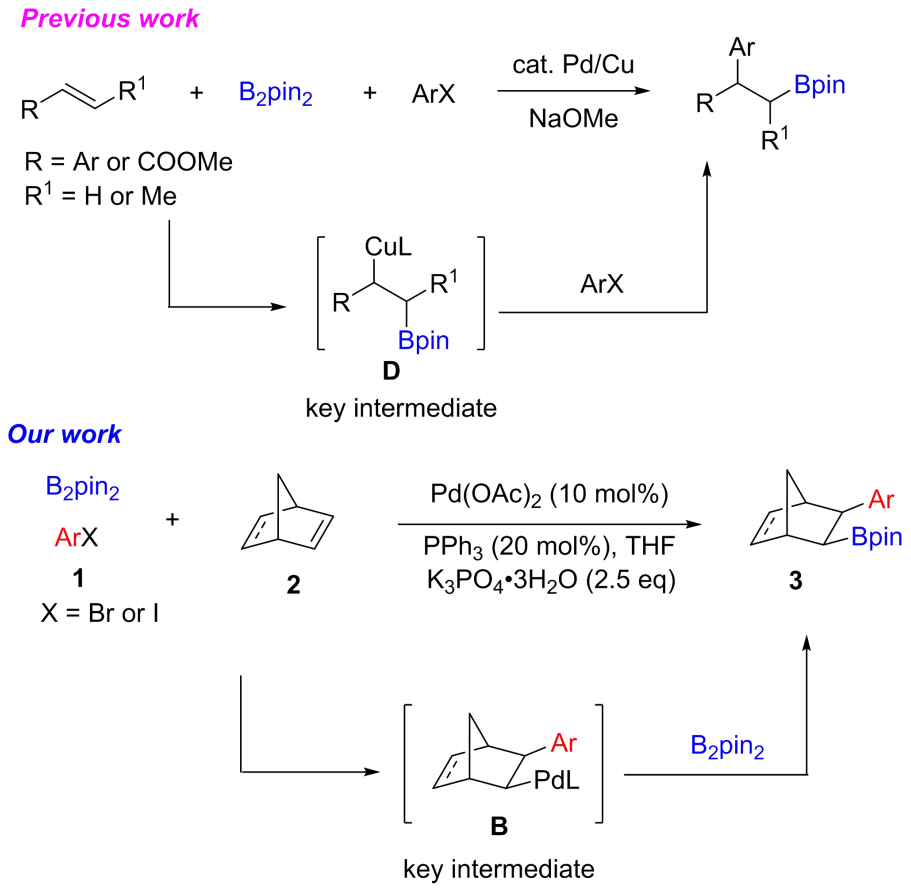
Transition-metal-catalyzed carboboration of alkenes has become an attractive and efficient strategy to access highly functionalized alkylboranes, which are versatile building blocks in organic synthesis and pharmaceuticals, from readily available starting materials.[1] A myriad of methods have been developed by intramolecular carboboration of alkenes catalyzed by Pd[2] or

Cu catalysts,[3] however, intermolecular carboboration of alkenes are relatively rare. Recently, several elegant works have been developed on this topic.[4] For instance, Cheng and his coworkers reported a Pd-catalyzed acylboration of 1,2-dienes with acyl chlorides and B_2pin_2;[4a] Toste *et al.* disclosed a palladium-catalyzed 1,1-arylborylation of terminal alkenes affording benzylic boronic esters;[4b] in 2014, Hoveyda and co-workers reported a multicomponent carboboration process involving 1,3-enynes, aldehydes and B_2pin_2;[4c] Yoshida *et al.* reported an efficient way to facilitate multi-functionalized alkylboranes;[4d] and Semba and Nakao *et al.* as well as Brown succeeded in the construction of 1,1-diarylalkanes boronates by an intermolecular arylboration of alkenes with aryl halide and B_2pin_2.[4e-g] Very recently Liao reported a Cu/Pd cooperative catalysis for enantioselective allyboration of alkenes.[4h] These reactions are remarkable since they provide efficient ways for difunctionalization of alkenes. And the majority of the precedent reports take advantage of Cu-Bpin complex, due to its ability to add to olefins, rendering an activated boronated Cu complex which could further react with electrophiles, such as aryl halides, alkyl halides, aldehydes etc. However, in all of the above known processes, activated alkenes, such as aryl alkenes, Bpin and $SiMe_2Ph$ alkenes have been explored; unactivated alkenes, especially cyclic alkenes, have not yet been developed as successful substrates for arylboration Inspired by Catellani-type reaction,[5-6] we envisaged that once intermediate **B** in Scheme 1 was formed, instead of further leading to the key intermediate of Catellani reaction (palladacycle **C** in Scheme 1), this intermediate **B** might directly undergo with a nucleophile, such as diboron compound, to generate the desired product via borylation reaction (Scheme 1).



Scheme 1. Proposed mechanism

We herein report a three-component arylboration of unactivated alkylalkenes, namely norbornene and norbornadiene, with either aryl iodides or aryl bromides and B_2pin_2 leading to fully functionalized alkylborane derivatives. Noteworthily, instead of proceeding in a tandem protocol via the cross-coupling of well-known β-borylalkylcopper intermediate (intermediate **D** in Scheme 2) with aryl halides as previous reports did,[4c-g] our strategy was based on a Catellani-type reaction, in which norbornene was inserted into the active arylpalladium intermediate to generate a new alkylpalladium intermediate **B** (Scheme 1 and 2), which was followed by borylation with B_2pin_2 to lead to the desired products.



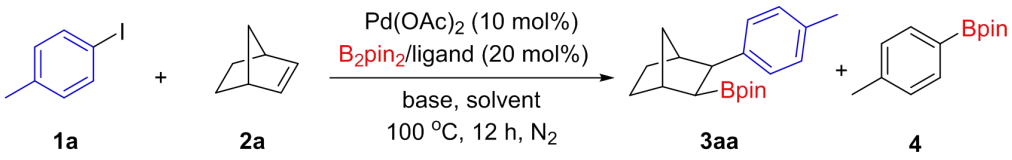
Scheme 2. Transition-metal-catalyzed arylboration of alkenes

RESULTS AND DISCUSSION

To evaluate our hypothesis, we commenced our study with 4-iodotoluene (**1a**) and norbornene (**2a**) as substrates using 10 mol% of $Pd(OAc)_2$ as the catalyst at 100 °C in toluene (Table 1). To our delight, the desired product **3aa** was formed in 48% isolated yield with PPh_3 as the ligand and Cs_2CO_3 as the base (Table 1, entry 1) along with trace amount of Suzuki-Miyaura borylative product **4**. Further ligand and base screening suggested that PPh_3 and $K_3PO_4•3H_2O$ were the optimal ones (Table 1, entries 1-11). The loading of B_2pin_2 affected the reaction dramatically, and with 1.5 equivalent of B_2pin_2, the desired product was obtained in 72% yield, which was in contrast to 60% yield obtained with 1.2 equivalent of B_2pin_2 and 50% yield observed with 1.0 equivalent of B_2pin_2 (Table 1, entries 4, 12-13). Subsequently, solvent

optimization demonstrated that THF was the best one among toluene, dioxane, CH_3CN and DMF (Table 1, entries 14-17). Fine tuning of the reaction procedure eventually revealed that premixing of the Pd catalyst and ligand with base is essential for the optimal result of 93% yield of this transformation (Table 1, entry 18). Control experiments without ligand or without Pd catalyst were performed accordingly, trace or poor results were obtained (Table 1, entries 19 and 20). As we can see, Miyaura borylation product did be formed under certain cases, and in some conditions which is even the main product (Table 1, entries 5, 9, 10 and 20). Interestingly, the aryl C-H activation product was not detected in most of cases, might be due to the kinetic effect.

Table 1. Optimization of the reaction parameters.



1a **2a** **3aa** **4**

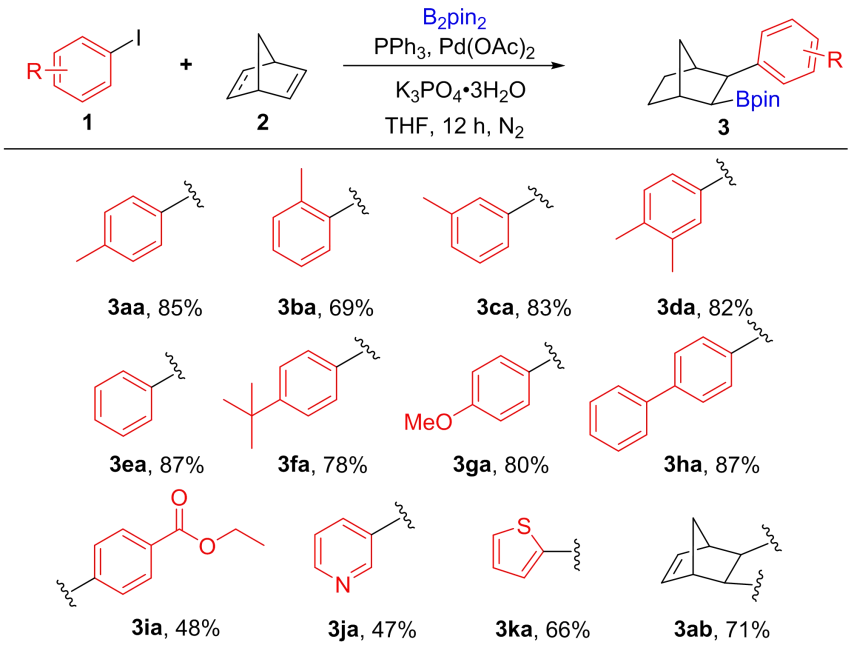
Entry	Ligand	Base	Solvent	yield of **3aa** (%)[e]	yield of **4** (%)
1	PPh_3	Cs_2CO_3	toluene	48	trace
2	PPh_3	K_2CO_3	toluene	23	16
3	PPh_3	Na_2CO_3	toluene	trace	trace
4	PPh_3	$K_3PO_4•3H_2O$	toluene	50	trace
5	PPh_3	K_2HPO_4	toluene	9	45
6	PCy_3	$K_3PO_4•3H_2O$	toluene	47	19
7	dppe	$K_3PO_4•3H_2O$	toluene	41	trace
8	dppf	$K_3PO_4•3H_2O$	toluene	45	0
9	$PtBu_3$	$K_3PO_4•3H_2O$	toluene	trace	58
10	S-phos	$K_3PO_4•3H_2O$	toluene	trace	67
11	X-phos	$K_3PO_4•3H_2O$	toluene	17	trace
12[b]	PPh_3	$K_3PO_4•3H_2O$	toluene	60	trace
13[c]	PPh_3	$K_3PO_4•3H_2O$	toluene	72	trace
14[c]	PPh_3	$K_3PO_4•3H_2O$	THF	89 (81)	0
15[c]	PPh_3	$K_3PO_4•3H_2O$	dioxane	31	0
16[c]	PPh_3	$K_3PO_4•3H_2O$	CH_3CN	53	trace
17[c]	PPh_3	$K_3PO_4•3H_2O$	DMF	25	17
18[c, d]	PPh_3	$K_3PO_4•3H_2O$	THF	93 (85)	0
19[c, d]	--	$K_3PO_4•3H_2O$	THF	0	0
20[c, d, f]	PPh_3	$K_3PO_4•3H_2O$	THF	12	52

Conditions: a) $Pd(OAc)_2$ (10 mol%), ligand (20 mol%), base (2.5 eq), solvent (3 mL), B_2pin_2 (1 eq); b) B_2pin_2 (1.2 eq); c) B_2pin_2 (1.5 eq); d) a sealed tube was charged with $Pd(OAc)_2$ (4.5 mg, 10 mol%) and ligand (10.5 mg, 20 mol%), base (2.5 eq) in THF (3 mL), and the resulting solution was stirred for 20 min at room temperature in N_2, then add others. e) GC yields with isolated yield in parenthesis; f) no $Pd(OAc)_2$.

With the optimized conditions in hand, we further turned our attention to the scope of this reaction (Scheme 3). Gratifyingly, a variety of aryl iodide derivatives which bear either electron-donating (methyl, *p*-tBu, *p*-MeO) or electron-withdrawing (*p*-phenyl, *p*-ester) groups on the aromatic rings were well tolerable in this transformation, affording the desired products in moderate to good yields (**3aa**-**3ka** in Scheme 3). Substituted toluenes gave the desired products in high yields as well with the *ortho* example giving a relatively low yield of 69% (**3aa**-**3ca**). Heteroaromatic iodides, such as 3-iodopyridine (**1j**) and 2-iodothiophene (**1k**)

worked smoothly under standard conditions to give desired products **3ja** and **3ka** in 47% and 66% yields, respectively. It was noteworthy that (**1s**,**4s**)-bicyclo[2.2.1]hepta-2,5-diene (**2b**) was also a suitable substrate in this transformation, generating corresponding alkene **3ab** in 71% yield (Scheme 3). Styrene and methyl acrylate were also tested under our standard condition, yet no desired products were generated or obtained.

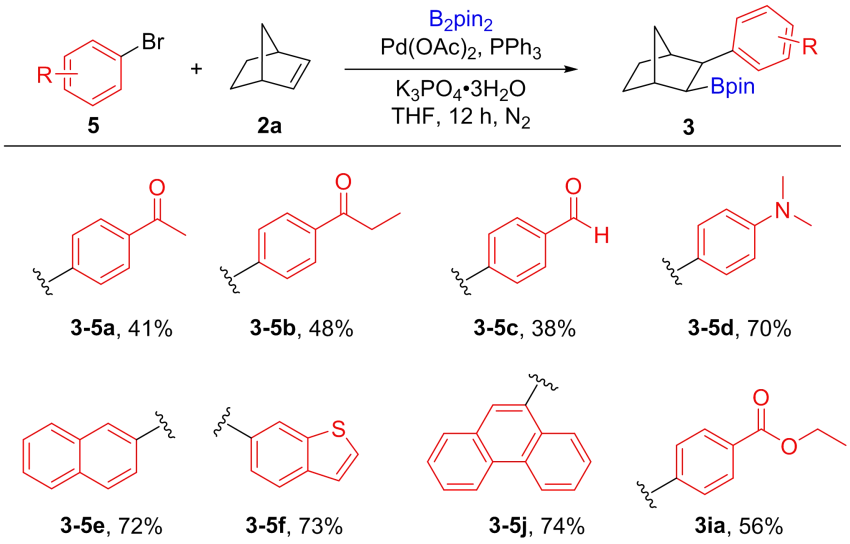
Scheme 3. Scope of Aryl Iodides.[a]



[a] Reaction conditions: **1** (0.2 mmol), **2** (2 eq), B_2pin_2 (1.5 eq), $Pd(OAc)_2$ (10 mol%), PPh_3 (20 mol%), $K_3PO_4•3H_2O$ (2.5 eq), THF (3 mL).

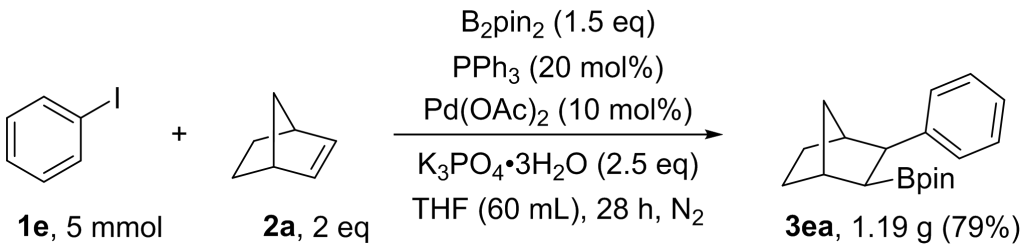
Various aryl bromides were subsequently investigated to explore the tolerability of the reaction as well under the optimized conditions. As shown in Scheme 4, the reaction worked very well with different functional groups on the aromatic rings of aryl bromides: ketones (**3-5a** and **3-5b**), aldehyde (**3-5c**) and ester (**3ia**) were all compatible under the standard conditions to lead to the desired products. The N, N-dimethylamino group was also a suitable substrate in addition to the polyphenylene aromatic ones (**3-5e** and **3-5j**) and heteroaromatic one (**3-5f**) and gave the desired products in ca. 70% yields (Scheme 4).

Scheme 4. Scope of Aryl Bromides.[a]



[a] Reaction condition: **5** (0.2 mmol), **2** (2 eq), B_2pin_2 (1.5 eq), $Pd(OAc)_2$ (10 mol%), PPh_3 (20 mol%), $K_3PO_4•3H_2O$ (2.5 eq), THF (3 mL).

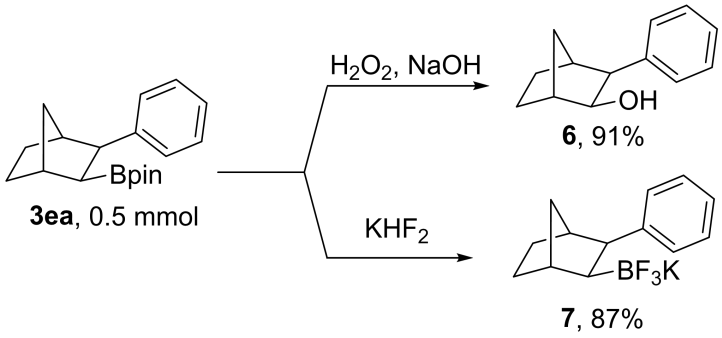
It is noteworthy that the reaction can be readily scaled up without loss of efficiency (Scheme 5): when **1e** (5 mmol) and **2a** (10 mmol) were exposed to the standard conditions, 79% (1.19 g) of desired product **3ea** was obtained (Scheme 4), which demonstrated the potential utility of this transformation to the synthetic community, since boron esters are widely used as a coupling partner in organic chemistry.[7]



Scheme 5. A Scale-up Experiment.

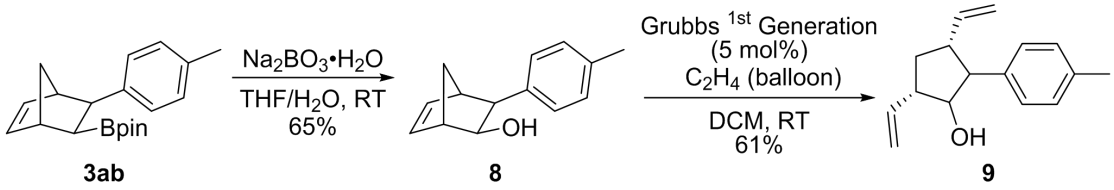
The synthetic utility of the β-borylated derivatives obtained by the present method was first emphasized by transformation of the boron substituent into various functional groups (Scheme 6). Bicyclic alcohol **6** and potassium bicyclic trifluoroborate **7**, which has been designated as one of the most important coupling partners in transition-metal-catalyzed

syntheses, were prepared from **3ea** in 91% and 87% yields, respectively. Surprisingly, Suzuki-Miyaura cross-coupling reactions were performed between **3ea** and iodobenzene and chlorobenzene respectively, yet neither of them gave desired products. These results suggest that the failure of Suzuki-Miyaura cross-coupling might stem from the steric hindrance of the reaction.



Scheme 6. Synthetic Transformation of 3ea.

Alkene **3ab**, made from (1s,4s)-bicyclo[2.2.1]hepta-2,5-diene (**2b**) and PhI with B_2pin_2 under the standard condition, was converted into corresponding alcohol **8** in 65% yield in the presence of $NaBO_3•H_2O$,[8] using the Grubbs 1st generation catalyst and ethylene atmosphere, the C=C bond of alcohol **8** was cleaved to give dialkene **9**,[9] which is readily transformed into various useful building blocks (Scheme 7).



Scheme 7. Olefin metathesis of 3ab.

CONCLUSIONS

In conclusion, a palladium-catalyzed arylboration of bicyclic alkenes with aryl halides and bis(pinacolato)diboron has been disclosed. This protocol is an alternative way to obtain

β-aryl alkylboronates and is complementary to existing methods to construct versatile multi-functionalized alkylboranates. A variety of functional groups are well tolerated in this transformation. Further exploration on the synthetic applications is under the way in our laboratory.

EXPERIMENTAL SECTION

General information. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification, THF was distilled from sodium/benzophenone. All experiments were conducted with a schlenk tube. Flash column chromatography was performed over silica gel (200-300 mesh). ^{1}H NMR spectra were recorded on a 500M NMR spectrometers, chemical shifts (in ppm) were referenced to $CDCl_3$ (δ = 7.26 ppm), DMSO-d_6 (δ = 2.50 ppm) as an internal standard. ^{13}C NMR spectra were obtained by using the same NMR spectrometers and were calibrated with $CDCl_3$ (δ = 77.0 ppm), DMSO-d_6 (δ = 39.6 ppm).

Note: The carbon directly attached to the boron atom is not detected because of quadrupolar relaxation. Therefore, that kind of carbon of the products cannot see in the ^{13}C spectra.

Procedure and characterization data for products. A sealed tube was charged with $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 10 mol%) and PPh_3 (10.5 mg, 0.04 mmol, 20 mol%), $K_3PO_4 \cdot 3H_2O$ (133.2 mg, 0.5 mmol, 2.5 eq) in THF (3 mL), and the resulting solution was stirred for 20 min at room temperature in N_2, then add aryl halide (0.2 mmol), norbornene or norbornadiene (0.4 mmol, 2 eq) and B_2pin_2 (76.2 mg, 0.3 mmol, 1.5 eq). The sealed tube was immersed in a oil bath at 100 °C. Upon completion, the reaction mixture was diluted with

ethyl acetate, filtered through a silica gel plug, rinsed with ethyl acetate, and concentrated in vacuo. The crude reaction mixture was purified on silica gel (petroleum ether: ethyl acetate = 50:1) to afford the desired product.

3aa，colorless oil, 53.0 mg (85% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.0 Hz, 2H), 2.95 (d, *J* = 10.5 Hz, 1H), 2.45 (s, 1H), 2.32 (s, 1H), 2.26 (s, 3H), 2.06 (d, *J* = 9.5 Hz, 1H), 1.65 – 1.59 (m, 2H), 1.56 (dd, *J* = 10.5, 2.0 Hz, 1H), 1.37 – 1.34 (m, 2H), 1.31-1.25 (m, 1H), 0.86 (s, 6H), 0.85 (s, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 143.1, 134.6, 128.5, 127.9, 82.4, 49.3, 41.4, 39.3, 37.7, 31.1, 31.1, 24.6, 24.5, 20.8. HRMS (Orbitrap, ESI, m/z) calcd for $[C20H29BO2+H]^+$: 313.2339; found: 313.2333.

3ba，colorless oil, 43.0 mg (69% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.0 Hz, 1H), 7.09-6.99 (m, 3H), 3.01 (d, *J* = 10.5 Hz, 1H), 2.52 (s, 1H), 2.33 (s, 3H), 2.15 (d, *J* = 9.5 Hz, 1H), 1.66-1.61 (m, 3H), 1.40-1.32 (m, 4H), 0.82 (s, 6H), 0.81 (s, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 144.3, 136.9, 129.9, 125.9, 125.4, 125.2, 82.2, 46.3, 40.9, 39.7, 37.7, 31.5, 31.2, 24.6, 24.4, 20.2. HRMS (Orbitrap, ESI, m/z) calcd for [C20H29BO2+H]: 313.2339; found: 313.2333.

3ca，colorless oil, 51.8 mg (83% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 – 7.04 (m, 3H), 6.90 (d, *J* = 7.4 Hz, 1H), 2.95 (d, *J* = 11.0 Hz, 1H), 2.48 (s, 1H), 2.33 (s, 1H), 2.29 (s, 3H), 2.09 (d, *J* = 10.0 Hz, 1H), 1.66 – 1.61 (m, 2H), 1.57 (dd, *J* = 10.5, 1.5 Hz, 1H),1.38-1.32 (m, 2H), 1.30 – 1.26 (m, 1H), 0.86 (s, 6H), 0.85 (s, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 146.0, 137.1, 129.0, 127.8, 126.0, 124.8, 82.3, 49.6, 41.2, 39.3, 37.7, 31.1, 31.1, 24.6, 24.5, 21.4. HRMS (Orbitrap, ESI, m/z) calcd for [C20H29BO2+H]: 313.2339; found: 313.2333.

3da，colorless oil, 53.5 mg (82% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.00 (s, 1H), 6.96 (s,

2H), 2.92 (d, *J* = 10.5 Hz, 1H), 2.45 (s, 1H), 2.32 (s, 1H), 2.20 (s, 3H), 2.17 (s, 3H), 2.07 (d, *J* = 9.5 Hz, 1H), 1.63 – 1.58 (m, 2H), 1.55 (dd, *J* = 10.5, 1.5 Hz, 1H), 1.36-1.31 (m, 2H), 1.29-1.26 (m, 2H), 0.86 (s, 6H), 0.84 (s, 6H).$^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 143.5, 135.6, 133.2, 129.6, 129.1, 125.1, 82.3, 49.3, 41.4, 39.2, 37.7, 31.2, 31.1, 24.6, 24.5, 19.7, 19.1. HRMS (TOF, EI, m/z) calcd for $[C21H31BO2+Na]^+$: 349.2315; found: 349.2306.

3ea，colorless oil, 51.8 mg (87%, yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25-7.19 (m, 4H), 7.10-7.07 (m, 1H), 2.99 (d, *J* = 10.5 Hz, 1H), 2.49 (s, 1H), 2.34 (s, 1H), 2.08 (d, *J* = 9.5 Hz, 1H), 1.66-1.58 (m, 3H), 1.39-1.33 (m, 2H), 1.30-1.26 (m, 1H), 0.85(s, 6H), 0.84(s, 6H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 146.1, 128.0, 127.9, 125.3, 82.4, 49.7, 41.2, 39.3, 37.7, 31.1, 31.1, 24.6, 24.6. HRMS (TOF, EI, m/z) calcd for [C19H27BO2+H]: 299.2182; found: 299.2177.

3fa，white solid, 55.2 mg (78%, yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.0 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 2.97 (d, *J* = 10.5Hz, 1H), 2.49 (s, 1H), 2.32 (s, 1H), 2.08 (d, *J* = 9.5 Hz, 1H), 1.61 – 1.56 (m, 3H), 1.39 – 1.31 (m, 3H), 1.27 (s, 9H), 0.83 (s, 6H), 0.83 (s, 6H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 148.0, 143.0, 127.6, 124.8, 82.3, 49.1, 41.1, 39.3, 37.8, 34.2, 31.4, 31.1, 24.6, 24.6. HRMS (TOF, EI, m/z) calcd for [C23H35BO2]: 354.2730; found: 354.2725.

3ga，colorless oil, 52.5 mg (80%, yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 (d, *J* = 9.0 Hz, 2H), 6.76 (d, *J* = 9.0 Hz, 2H), 3.75 (s, 3H), 2.93 (d, *J* = 10.5 Hz, 1H), 2.43 (s, 1H), 2.32 (s, 1H), 2.05 (d, *J* = 9.5 Hz, 1H), 1.64 – 1.58 (m, 3H), 1.55 – 1.53 (m, 1H), 1.36 – 1.32 (m, 2H), 1.28-1.25 (m, 1H), 0.88 (s, 6H), 0.86 (s, 6H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 157.5,

138.5, 128.9, 113.4, 82.4, 55.4, 48.9, 41.6, 39.3, 37.6, 31.1, 31.1, 24.7, 24.6. HRMS (Orbitrap, ESI, m/z) calcd for [C20H29BO3+H]: 329.2288; found:329.2282.

3ha， white solid, 65.1 mg (87%, yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 – 7.51 (m, 2H), 7.45 – 7.41 (m, 4H), 7.33 – 7.31 (m, 3H), 3.03 (d, *J* = 10.5 Hz, 1H), 2.53 (s, 1H), 2.36 (s, 1H), 2.11 (d, *J* = 10.0 Hz, 1H), 1.64-1.60 (m, 3H), 1.43 – 1.36 (m, 2H), 1.32 – 1.29 (m, 1H), 0.86 (s, 6H), 0.85(s, 6H).^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 145.3, 141.5, 138.4, 128.6, 128.4, 126.9, 126.8, 126.7, 82.5, 49.4, 41.3, 39.4, 37.8, 31.1, 31.1, 24.6, 24.5. HRMS (TOF, EI, m/z) calcd for [C25H31BO2]: 374.2417; found: 374.2423.

3ia， colorless oil, ethyl 4-iodobenzoate as substrate, 35.5 mg (48%, yield); ethyl 4-bromobenzoate as substrate, 41.4 mg, (56%, yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 8.5 Hz, 2H), 4.34 (q, *J* = 7.0 Hz, 2H), 3.01 (d, *J* = 10.5 Hz, 1H), 2.48 (s, 1H), 2.34 (s, 1H), 2.04 (d, *J* = 9.5 Hz, 1H), 1.65-1.60 (m, 3H), 1.37 (t, *J* = 7.0 Hz, 3H), 1.31 – 1.23 (m, 3H), 0.83 (s, 6H), 0.83 (s, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 166.8, 151.7, 129.2, 128.0, 127.5, 82.5, 60.6, 49.8, 41.2, 39.4, 37.7, 31.0, 31.0, 24.6, 24.5, 14.31. HRMS (Orbitrap, ESI, m/z) calcd for [C22H31BO4+H]: 371.2394; found: 371.2388.

3ja，yellow oil, 28.1 mg (47%, yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (s, 1H), 8.33 (d, *J* = 4.0 Hz, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.13 (dd, *J* = 8.0, 5.0 Hz, 1H), 2.96 (d, *J* = 10.5 Hz, 1H), 2.47 (s, 1H), 2.36 (s, 1H), 2.00 (d, *J* = 10.0 Hz, 1H), 1.65-1.58 (m, 3H), 1.40 – 1.29 (m, 3H), 0.85 (s, 6H), 0.84 (s, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 149.8, 146.5, 141.5, 135.3, 122.9, 82.6, 47.3, 41.1, 39.4, 37.7, 31.0, 31.0, 24.6, 24.5. HRMS (Orbitrap, ESI, m/z) calcd for [C18H26BNO2+H]: 300.2135; found: 300.2129.

3ka，light yellow oil, 40.1 mg (66%, yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.01 (dd, *J* = 5.0, 1.0 Hz, 1H), 6.85 – 6.82 (m, 2H), 3.24 (d, *J* = 10.5 Hz, 1H), 2.45 (s, 1H), 2.38 (s, 1H), 2.10 (d, *J* = 10.0 Hz, 1H), 1.64 – 1.51 (m, 3H), 1.38 – 1.31 (m, 2H), 1.27-1.22 (m, 1H), 0.98 (s, 6H), 0.93 (s, 6H). ^{113}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 150.2, 126.3, 123.5, 121.9, 82.5, 45.4, 44.1, 39.2, 37.6, 31.0, 30.5, 24.9, 24.6. HRMS (Orbitrap, ESI, m/z) calcd for [C17H25BO2S+H]: 305.1741; found: 305.1747.

3ab，colorless oil, 44.0 mg (71%, yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.14 (d, *J* = 8.0 Hz, 2H), 7.04 (d, *J* = 8.0 Hz, 2H), 6.24-6.18(m, 2H), 2.97 (s, 1H), 2.91 (s, 1H), 2.82 (d, *J* = 10.5 Hz, 1H), 2.28 (s, 3H), 2.05 (d, *J* = 8.5 Hz, 1H), 1.50(d, *J* = 8.5 Hz, 1H), 1.33-1.28 (m, 2H), 0.87 (s, 6H), 0.86 (s, 6H).^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 141.6, 138.6, 137.3, 134.8, 128.5, 128.3, 82.6, 46.8, 46.5, 45.9, 44.6, 24.6, 20.8. HRMS (TOF, EI, m/z) calcd for [C16H25BO2]: 260.1948; found: 260.1950.

3-5a, white solid, 27.9 mg (41%, yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.5 Hz, 2H), 7.32 (d, *J* = 8.5 Hz, 2H), 3.02 (d, *J* = 11.0 Hz, 1H), 2.54 (s, 3H), 2.49 (s, 1H), 2.34 (s, 1H), 2.03 (d, *J* = 10.0 Hz, 1H), 1.65-1.59 (m, 3H), 1.39-1.34 (m, 2H), 1.31-1.27 (m, 1H), 0.82 (s, 12H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 197.9, 152.2, 134.5, 128.2, 128.1, 82.5, 49.8, 41.1, 39.4, 37.7, 31.0, 31.0, 26.5, 24.6, 24.5. HRMS (Orbitrap, ESI, m/z) calcd for [C21H29BO3+H]: 341.2288; found: 341.2282.

3-5b, white solid, 34.0 mg (48%, yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 3.01 (d, *J* = 11.0 Hz, 1H), 2.94 (q, *J* = 7.0 Hz, 2H), 2.49 (s, 1H), 2.34 (s, 1H), 2.04 (d, *J* = 7.0 Hz, 1H), 1.67 – 1.59 (m, 3H), 1.39 – 1.30 (m, 3H), 1.19 (t, *J* = 7.0 Hz, 3H), 0.82 (s, 12H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 200.7, 151.9, 134.2, 128.2,

127.8, 82.5, 49.8, 41.1, 39.4, 37.7, 31.7, 31.0, 30.9 24.6.24.5, 8.4. HRMS (Orbitrap, ESI, m/z) calcd for [C22H31BO3+H]: 355.2445; found: 355.2439.

3-5c, white solid, 24.8 mg (38%, yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.93 (s, 1H), 7.73 (d, *J* = 8.5 Hz, 2H), 7.39 (d, *J* = 8.5 Hz, 2H), 3.04 (d, *J* = 11.0 Hz, 1H), 2.51 (s, 1H), 2.36 (s, 1H), 2.04 (d, *J* = 9.5 Hz, 1H), 1.66 – 1.62 (m, 4H), 1.41-1.30 (m, 3H), 0.82 (s, 12H). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 192.1, 153.9, 134.0, 129.6, 128.7, 82.6, 50.0, 41.0, 39.5, 37.6, 31.0, 31.0, 24.6, 24.5. HRMS (Orbitrap, ESI, m/z) calcd for [C20H27BO3+H]: 327.2132; found: 327.2126.

3-5d, light brown solid, 47.7 mg (70%, yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.5 Hz, 2H), 6.66 (d, *J* = 8.5 Hz, 2H), 2.91 (d, *J* = 10.5 Hz, 1H), 2.84 (s, 6H), 2.43 (s, 1H), 2.31 (s, 1H), 2.06 (d, *J* = 10.0 Hz, 1H), 1.64 – 1.57 (m, 2H), 1.53 (dd, *J* = 10.5, 2.0 Hz, 1H), 1.35 – 1.31 (m, 2H), 1.27 – 1.24 (m, 1H), 0.88 (s, 6H), 0.86 (s, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 149.2, 135.2, 128.5, 113.4, 82.3), 48.8, 41.6, 41.4, 39.2, 37.7, 31.1, 24.7, 24.6. HRMS (Orbitrap, ESI, m/z) calcd for [C21H32BNO2+H]: 342.2604; found: 342.2599.

3-5e, white solid, 50.1 mg (72%, yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76-7.73 (m, 2H), 7.70-7.67 (m, 2H), 7.41 – 7.35 (m, 3H), 3.15 (d, *J* = 10.5 Hz, 1H), 2.61 (s, 1H), 2.39 (s, 1H), 2.20 (d, *J* = 9.5 Hz, 1H), 1.72-1.66 (m, 3H), 1.45-1.33 (m, 3H), 0.68 (s, 12H). ^{13}C{^{1}H} NMR (125MHz, $CDCl_3$) δ 143.7, 133.5, 131.8, 127.6, 127.5, 127.3, 127.2, 125.5, 125.4, 124.7, 82.3, 49.8, 41.4, 39.4, 37.8, 31.2, 24.5. HRMS (TOF, EI, m/z) calcd for [C23H29BO2]: 348.2261; found: 348.2266.

3-5f, colorless oil, 51.7 mg (73%, yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71-7.69 (m, 2H), 7.36 (d, *J* = 5.0 Hz, 1H), 7.26 – 7.23 (m, 2H), 3.12 (d, *J* = 11.0 Hz, 1H), 2.56 (s, 1H), 2.36 (s,

1H), 2.16 (d, J = 10.0 Hz, 1H), 1.69 – 1.62 (m, 3H), 1.39– 1.31 (m, 3H), 0.73 (s, 6H), 0.71 (s, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 142.4, 139.7, 136.8, 125.9, 125.4, 123.8, 122.4, 121.7, 82.3, 49.6, 41.5, 39.4, 37.9, 31.2, 31.1 24.5, 24.4. HRMS (TOF, EI, m/z) calcd for [C21H27BO2S]: 354.1825; found: 354.1822.

3-5j, white solid, 58.9 mg (74%, yield). ^1H NMR (500 MHz, $CDCl_3$) δ 8.68 – 8.66 (m, 1H), 8.61-8.59 (m, 1H), 8.20-8.18 (m, 1H), 7.86 – 7.85 (m, 1H), 7.69 (s, 1H), 7.64 – 7.59 (m, 2H), 7.56 – 7.54 (m, 2H), 3.59 (d, J = 10.5 Hz, 1H), 2.86 (d, J = 3.5 Hz, 1H), 2.38 (d, J = 3.5 Hz, 1H), 2.30 (d, J = 9.5 Hz, 1H), 1.89 – 1.87 (m, 1H), 1.55 – 1.46 (m, 2H), 0.40 (m, 6H), 0.38 (m, 6H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 140.0, 132.0, 131.7, 130.7, 129.2, 128.4, 126.2, 126.2, 125.8, 125.5, 125.4, 123.2, 122.7, 122.1, 81.9, 45.9, 40.5, 40.1, 37.38 (s), 31.7, 31.1, 24.0, 23.9. HRMS (TOF, EI, m/z) calcd for [C27H31BO2]: 398.2417; found: 398.2420.

Compound 6，The product **6** was prepared according to a reported procedure.[10] Boronic ester **3ea** (149 mg, 0.5 mmol) was dissloved in THF (1 mL). The solution was cooled to 0 °C, followed by the dropwise addition of 3 M sodium hydroxide (0.5 mL) and 30% aqueous H_2O_2 (0.5 mL). The reaction was allowed to slowly warm to room temperature while stirring for at least 4 h. The reation was c quenched with aqueous $Na_2S_2O_3$. The aqueous later was extracted with ethyl acetate. The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude material was purified on silica gel to afford the desired product **6** as colorless oil (86 mg, 91%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.35 – 7.31 (m, 2H), 7.26 – 7.21 (m, 3H), 3.98 – 3.96 (m, 1H), 2.93 (d, J = 7.0 Hz, 1H), 2.50 (s, 1H), 2.34 (d, J = 5.0 Hz, 1H), 2.02 (d, J = 10.0 Hz, 1H), 1.67 – 1.53 (m, 2H), 1.33-1.27 (m, 2H), 1.24 – 1.19

(m, 1H), 0.95 (s, 1H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 138.9, 128.9, 128.5, 126.5, 76.8, 54.5, 43.3, 40.5, 34.6, 30.4, 23.9.

Compound 7，The product **7** was prepared according to a reported procedure.[11] Boronic ester **3ea** (149 mg, 0.5 mmol) was dissloved in methanol (3 mL). To the solution was added KHF_2 (0.5 mL, 4.5 M aqueous solution, 2.25 eq) dropwise. The reaction mixture stirred at 25 ºC for 30 min. The solvent was then removed under vacuum and the solid residue was dissloved with acetone (3 mL). The liquid phase was filtered, and the solid residue was washed with additional acetone (3×1 mL). The combined solution was concentrated in vacuo to give white solid. The solids was washed with ether (3×2 mL) and dried under vacuum, affording the desired product **7** as white solid (121 mg, 87%). ^{1}H NMR (500 MHz, DMSO) δ 7.16 – 7.12 (m, 2H), 7.06-7.02 (m, 2H), 6.94 – 6.91 (m, 1H), 2.59 (d, J = 10.5 Hz, 1H), 2.12 (s, 1H), 2.03 (s, 1H), 1.90 (d, J = 9.0 Hz, 1H), 1.50 – 1.42 (m, 2H), 1.21 – 1.13 (m, 2H), 0.97 (d, J = 9.0 Hz, 1H), 0.79-0.74 (m, 1H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 149.1, 129.4, 127.4, 124.6, 51.7, 44.4, 37.1, 33.3, 32.1. HRMS (Orbitrap, ESI, m/z) calcd for [C13H15BF3]: 239.1219; found: 239.1224.

Compound 8，The product **8** was prepared according to a reported procedure.[12] Boronic ester 3ea (149 mg, 0.5 mmol) was dissloved in THF/H_2O (3 mL/3 mL). $NaBO_3$•H_2O (700 mg, 14 eq) was added to the solution in one portion, the resulting mixture was stirred for 24 h. The reaction was quenched with aqueous $Na_2S_2O_3$. The aqueous later was extracted with ethyl acetate. The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude material was purified on silica gel to afford the desired product **8** as colorless oil (65 mg, 65%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18-7.13 (m, 4H), 6.42 – 6.41 (m,

1H), 6.14-6.13 (m, 1H), 4.01 (d, J = 6.5 Hz, 1H), 3.02 (s, 1H), 2.95 (d, J = 7.0 Hz, 1H), 2.90 (s, 1H), 2.35 (d, J = 2.0 Hz, 3H), 2.12 (d, J = 9.0 Hz, 1H), 1.72 (dd, J = 9.0, 1.5 Hz, 1H), 1.45 (d, J = 3.0 Hz, 1H), 1.31-1.24 (m, 2H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 141.9, 136.2, 136.1, 134.9, 129.4, 128.8, 72.4, 49.4, 49.0, 45.2, 44.7, 20.9. HRMS (TOF, EI, m/z) calcd for $[C14H16O+Na]^+$: 223.1099; found: 223.1096.

Compound 9 , The product **9** was prepared according to a reported procedure.[13] In a glove-box filled with nitrogen, Grubbs 1st Generation catalyst (11 mg, 5 mol%) was placed in a schlenk tube, and the tube was taken outside the glove-box. The tube was filled with C_2H_4 gas. A solution of **7** (50 mg, 0.25 mmol) in CH_2Cl_2(1.5 mL) was added, and the solution was then stirred ambient temperature for additional 14 h under C_2H_4 (1 atm, balloon). The reaction was quenched with water. The aqueous later was extracted with ethyl acetate. The organic layers were combined, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude material was purified on silica gel to afford the desired product **9** as colorless oil (35 mg, 61%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.15 (s, 4H), 5.93 (ddd, J = 17.4, 10.3, 7.5 Hz, 1H), 5.71 (ddd, J = 17.4, 10.3, 7.4 Hz, 1H), 5.13 (d, J = 17.1 Hz, 1H), 5.04 (d, J = 10.3 Hz, 1H), 5.00 (d, J = 17.1 Hz, 1H), 4.90 (d, J = 10.3 Hz, 1H), 3.99 (s, 1H), 3.11 (ddd, J = 18.0, 10.8, 7.3 Hz, 1H), 2.90 (dd, J = 11.4, 5.8 Hz, 1H), 2.73-2.67 (m, 1H), 2.33 (s, 3H), 2.30 – 2.24 (m, 1H), 1.46 (ddd, J = 13.0, 10.3, 8.9 Hz, 1H), 1.33-1.25 (m, 1H). $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 140.7, 140.6, 136.5, 134.7, 129.3, 129.2, 114.6, 114.1, 80.5, 56.0, 50.5, 45.4, 36.5 21.0. HRMS (TOF, EI, m/z) calcd for [C16H20O]: 228.1514; found: 228.1518.

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SUPPORTING INFORMATION

^{1}H NMR and ^{13}C NMR spectra of New Compounds.

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