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Cross-coupling reactions of primary alkylboronic acids with aryl triflates and aryl halides

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Abstract—The cross-coupling reactions of primary alkylboronic acids with aryl triflates and aryl halides has been successfully achieved using $PdCl_2(dppf)\cdot CH_2Cl_2$ in the presence of potassium carbonate to provide the corresponding Suzuki coupled products in high yields.

1. Introduction

The palladium-catalyzed cross-coupling reaction of aryl triflates and aryl halides with organoboron compounds has emerged as a powerful method for carbon–carbon bond formation.[1,2] Among all possible organometallics, tin (Stille coupling)[3,4] and boron derivatives (Suzuki coupling)[5–7] are most frequently used for cross-coupling reactions because of their tolerance of a broad range of functional groups. The use of organoboron derivatives is especially valued for several reasons: they are more easily accessed by a variety of routes, nontransferable groups can be readily incorporated into the organometallic, and the inorganic byproducts of the reaction are nontoxic and can be readily removed by simple workup procedures.

Trialkylboranes have been employed extensively in the Suzuki cross coupling reactions.[1,2,5,6] The most widely utilized trialkylboranes are the 9-BBN derivatives. These are enormously successful in general, but there are some drawbacks. For example, the alkyl-9-BBN compounds are extremely air-sensitive, and therefore difficult to isolate and purify. Typically the cross coupling is carried out in situ immediately after olefin hydroboration. Thus there is no opportunity to purify the organoboron intermediate in the event the hydroboration reaction has not proceeded well. The difficulty involved in isolating the organoboron would appear to limit their application in combinatorial library synthesis as well. Some functional groups (ketones, for example) must be protected during the 9-BBN hydroboration. This is not the case for rhodium-catalyzed catecholborane hydroborations.[8] Further, coupling reactions using 9-BBN derivatives are not atom economic, as the cyclooctyl unit must be disposed of after the cross coupling. Finally, in some instances stereocomplementary hydroborations can be achieved under rhodium-catalyzed conditions as compared to those carried out with 9-BBN.[9–11] For all of these these reasons, it is imperative to consider alternative organoboron reagents for Suzuki coupling reactions.

In one such procedure, methylation reactions have been carried out using Suzuki coupling of methylborinate esters.[12,13] These reagents couple with a variety of electrophilic substrates, but their synthesis is a bit involved. Additionally, extrapolation to other alkylborinates has not been demonstrated and this approach does not deal with the issue of atom economy.

Except for the recent example of cyclopropylboronic acids or -esters that possess significant sp^2-carbon character,[14,15] more highly oxygenated derivatives such as alkylboronic acids or -esters have presented difficulties in Suzuki coupling reactions. An early study utilizing alkylboronic acids provided the coupled products in only 20–30% yield,[16] while coupling of methylboronic acid required the addition of 40 mol% of triphenylarsine.[17] More recent studies show promise of improving this situation, although the scope of this particular protocol has not been fully investigated.[18] A similar situation exists for various alkylboronic esters, where very low yields in the cross-coupling reaction have been obtained[19] unless highly toxic[20] thallium compounds such as TlOH or Tl_2CO_3 were utilized as bases for the reaction.[21] It has been assumed that this is because of the difficulty in transmetalation between the boronic ester and the intermediate Pd species. Thus, although Suzuki coupling reactions incorporating aryl- and alkenylboron reagents are reasonably well in hand, new and effective methods for the successful coupling of simple primary

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Table 1. Cross-coupling reactions of alkylboronic acids with aryl triflates

Entry	Boronic acid	Triflate	Product	% Yield
1	$PhCH_2CH_2B(OH)_2$ (**1a**)	TfOPh*p*-Ac	Ph*p*-Ac (**2a**)	91[a](97[b])
2	(**1a**)	TfOPh*p*-NO_2	Ph*p*-NO_2 (**2b**)	93[a]
3	$PhCH_2CH_2B(OH)_2$ (**1b**)	TfOPh*p*-Ac	Ph*p*-Ac (**2c**)	93[a] (94[b])
4	(**1b**)	TfOPh*p*-NO_2	Ph*p*-NO_2 (**2d**)	94[a]
5	(**1a**)	TfOPh*p*-Cl	Ph*p*-Cl (**2e**)	94[b]
6	(**1a**)	TfOPh*m*-CN	Ph*m*-CN (**2f**)	93[b]
7	(**1a**)	TfOPh*m*-CF_3	Ph*m*-CF_3 (**2g**)	92[b]
8	$CH_3B(OH)_2$ (**1c**)	TfOPh*p*-Ac	CH_3Ph*p*-Ac (**2h**)	85[b]
9	(**1c**)	TfOPh*p*-NO_2	CH_3Ph*p*-NO_2 (**2i**)	80[b]
10	(**1a**)	TfOPh*p*-OCH_3	Ph*p*-OCH_3 (**2j**)	15[b]

[a] Condition A: $PdCl_2$(dppf·CH_2Cl_2 (9 mol%), Cs_2CO_3 (3 equiv.), THF/H_2O (10/1), reflux.
[b] Condition B: $PdCl_2$(dppf·CH_2Cl_2 (9 mol%), K_2CO_3 (3 equiv.), THF/H_2O (10/1), reflux.

alkylboron species are still subject to significant improvement.

We recently published the cross-coupling reaction of potassium alkyltrifluoroborates with aryl- or alkenyl triflates.[22] The cross-coupling reaction worked smoothly, providing satisfactory yields of the coupled products in most cases. The reaction was tolerant of a variety of functional groups including ketones, esters, nitriles, and nitro groups despite the aqueous basic conditions. These alkyltrifluoroborates are usually considered more reactive than boronic acids.[23–26]

In the present study we have investigated the reactivity of alkylboronic acids in Suzuki coupling reactions. Herein, we outline the scope of the cross-coupling reaction of these substrates with aryl triflates and aryl halides as the coupling partner (Eq. (1)).

$$\text{R-B(OH)}_2\ (\text{R = alkyl}) + \begin{matrix}\text{ArOTf}\\ \text{or}\\ \text{ArX}\end{matrix} \xrightarrow[\text{THF-H}_2\text{O, reflux}]{\text{PdCl}_2(\text{dppf})\cdot\text{CH}_2\text{Cl}_2,\ \text{K}_2\text{CO}_3} \text{R-Ar} \qquad (1)$$

2. Results and discussion

The requisite alkylboronic acids were easily synthesized using established literature protocols involving the addition of Grignard reagents to trimethylborate,[27] or the hydroboration of alkenes with dibromoborane–dimethylsulfide complex followed by hydrolysis.[28] As a starting point, the conditions for carrying out the coupling reactions were the same as those previously optimized for the Suzuki coupling of alkyltrifluoroborates. Under these conditions the cross-coupling reactions of alkylboronic acids with various aryl triflates proceeded readily with high yields in most cases as outlined in Table 1.

Surprisingly, the high yields of the cross-coupling reaction were maintained when potassium carbonate was used as a base instead of cesium carbonate (entries 1 and 3). Also, the yields of the reaction with various aryl triflates were high regardless of the position of the functional group on the ring. However, the use of the electron rich 4-methoxyphenyltriflate provided the desired coupled product in only 15% yield (entry 10). As in the case of the alkyltrifluoroborate chemistry, nitro groups can be tolerated in the aryl triflate substrate (entries 2, 4, and 9). It has been reported that B-alkyl-9-BBN cross-couplings provide mixtures of reduced anilines in these cases.[29]

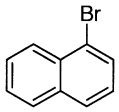
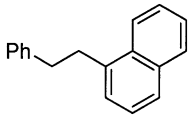
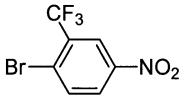
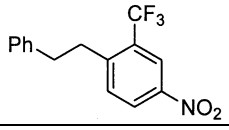
Catalyst loadings were typically quite high in these reactions (9 mol%). To explore the possibility of a lower catalyst loading, we examined the cross-coupling reaction of 2-phenylethylboronic acid (**1a**) with 4-acetylphenyltriflate using only 5 and 2 mol% of the palladium catalyst. Unfortunately, the yield of coupled product decreased to 48 and 25%, respectively.

Significantly, using the conditions developed we were able to obtain higher yields for methylation than in many of those procedures reported previously.[17,30–32] Thus, the coupling reaction of methylboronic acid with 4-acetyl- and 4-nitrophenyltriflate provided the desired coupled products in 85 and 80% yield, respectively (entries 8 and 9).

We have conducted several coupling reactions with various aryl bromides to compare their reactivity with that of aryl triflates (Table 2). As outlined in Table 2, the cross-coupling reaction with aryl bromides provided the coupled products with satisfactory yields in most cases, except for the electron rich 4-bromoanisole (entry 1). A similar result was observed when 4-methoxyphenyltriflate was used (entry 10, Table 1).

We have examined several different reaction conditions in an attempt to increase the reactivity of this coupling reaction. The use of THF without water produced an increase in the yield of the desired products (entries 9 and 10, Table 1). Surprisingly, the cross-coupling reaction of 4-bromobenzophenone and 4-bromobenzonitrile worked in good yield

Table 2. Cross-coupling reactions of phenylethylboronic acid with aryl bromides

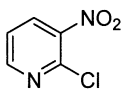
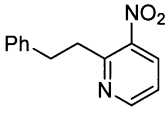
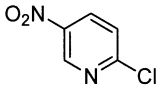
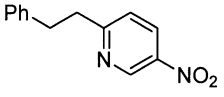
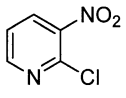
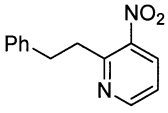
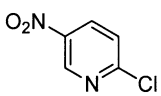
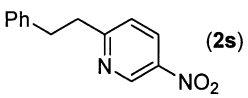
Entry	Boronic acid	Bromide	Product	% Yield
1	$PhCH_2CH_2B(OH)_2$ (**1a**)	Br*p*-OCH_3	Ph, *p*-OCH_3 (**2j**)	42[a]
2	(**1a**)	BrPh	Ph, Ph (**2k**)	73[a]
3	(**1a**)		 (**2l**)	73[a]
4	(**1a**)	Br*o*-CH_3	Ph, *o*-CH_3 (**2m**)	80[a]
5	(**1a**)	Br*p*-Ac	Ph, *p*-Ac (**2a**)	87[a] (71[b])
6	(**1a**)	Br*p*-CF_3	Ph, *p*-CF_3 (**2n**)	67[a]
7	(**1a**)	Br*p*-NO_2	Ph, *p*-NO_2 (**2b**)	53[a] (67[c], 60[d])
8	(**1a**)	Br*p*-COPh	Ph, *p*-COPh (**2o**)	64[a] (80[c])
9	(**1a**)	Br*p*-CN	Ph, *p*-CN (**2p**)	60[a] (79[e], 72[f])
10	(**1a**)		 (**2q**)	61[a] (64[e], 63[f])

[a] Condition B: $PdCl_2$ (dppf)·CH_2Cl_2 (9 mol%), K_2CO_3 (3 equiv.), THF/H_2O (10/1), reflux.
[b] 1,4-Dioxane/H_2O was used as a solvent.
[c] Condition D: $Pd(PPh_3)_4$ (10 mol%), K_2CO_3 (3 equiv.), 1,4-dioxane, reflux.
[d] Condition E: $PdCl_2$ (dppf)·CH_2Cl_2 (9 mol%), K_2CO_3 (3 equiv.), 1,4-dioxane, reflux.
[e] Condition C: $PdCl_2$ (dppf)·CH_2Cl_2 (9 mol%), K_2CO_3 (3 equiv.), THF, reflux.
[f] Condition F: $Pd_2(dba)_3$ (10 mol%), dppf (15 mol%), Cs_2CO_3 (3 equiv.), 1,4-dioxane, reflux.

even though $Pd(PPh_3)_4$ was used as the catalyst (entries 7 and 8). Of importance in this case was that we did not observe β-hydride elimination processes in any of the examples we have studied. Additionally, we obtained high yields when $Pd_2(dba)_3$ was used to generate the homogeneous catalyst (entries 9 and 10).

Finally, we have investigated the cross-coupling reaction of a few heteroaryl chlorides and **1a**. The results of these reactions are displayed in Table 3. The cross-coupling reaction of heteroaryl chlorides did not work under our standard conditions or when $Pd_2(dba)_3$/dppf was used as a catalyst instead of $PdCl_2$(dppf)·CH_2Cl_2 (entries 1 and 2). However,

Table 3. Cross-coupling reactions of phenylethylboronic acid with heteroaryl chlorides

Entry	Boronic acid	Aryl chloride	Product	% Yield
1	$PhCH_2CH_2B(OH)_2$ (**1a**)			NR[a,b]
2	(**1a**)			NR[a,b]
3	(**1a**)		 (**2r**)	52[c]
4	(**1a**)		 (**2s**)	53[c] (53[d])

[a] Condition B: $PdCl_2$ (dppf)·CH_2Cl_2 (9 mol%), K_2CO_3 (3 equiv.), THF/H_2O (10/1), reflux.
[b] Condition F: $Pd_2(dba)_3$ (10 mol%), dppf (15 mol%), Cs_2CO_3 (3 equiv.), 1,4-dioxane, reflux.
[c] Condition D: $Pd(PPh_3)_4$ (10 mol%), K_2CO_3 (3 equiv.), 1,4-dioxane, reflux.
[d] Condition C: $PdCl_2$(dppf)·CH_2Cl_2 (9 mol%) K_2CO_3 (3 equiv.), THF, reflux.

in non-aqueous solvent systems and using either $Pd(PPh_3)_4$ or $PdCl_2(dppf)\cdot CH_2Cl_2$ as the catalyst, the reaction proceeded to give moderate yields of the desired coupled products (entries 3 and 4).

In summary, the palladium-catalyzed cross-coupling reaction of primary alkylboronic acids with various aryl triflates and aryl halides has been achieved without resorting to toxic ligands or bases. Additionally, we have determined that alkylboronic acids can be coupled under diverse catalytic conditions without the interference of β-hydride elimination products.

3. Experimental

3.1. General

All experiments were carried out under an inert atmosphere. ^1H and ^{13}C NMR spectra were measured on spectrometers at 500.13 and 125.77 MHz, respectively. Palladium catalysts, Cs_2CO_3, 4-acetylphenyltriflate, 4-nitrophenyltriflate, 4-methoxyphenyltriflate, 4-bromoanisole, 4-bromobenzene, 4-bromoacetophenone, 1-bromonaphthalene, 4-bromobenzotrifluoride, 4-bromonitrobenzene, 4-bromobenzophenone, 4-bromobenzonitrile, 2-bromo-5-nitrobenzotrifluoride, 3-nitro-2-chloropyridine, 5-nitro-2-chloropyridine, and methylboronic acid were obtained from Aldrich. The triflates, 2-phenylethylboronic acid (**1a**), and 3-phenylpropylboronic acid (**1b**) were prepared by reported procedures.[33–35] All of the coupling reactions were performed on a 0.5 mmol scale.

3.1.1. Representative procedure A for the cross-coupling reaction of alkylboronic acids with aryl triflates. 1-(4-Acetylphenyl)-2-phenylethane (2a). To a suspension of 2-phenylethylboronic acid (**1a**) (75 mg, 0.50 mmol), Cs_2CO_3 (489 mg, 1.50 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (36 mg, 0.045 mmol), and 4-acetylphenyltriflate (148 mg, 0.55 mmol) in THF (5 mL) was added water (0.5 mL) under an argon atmosphere. The reaction mixture was stirred at reflux temperature for 18 h, then cooled to rt, diluted with water (10 mL), then extracted with ether (20 mL×3). The combined organic layers were washed with 1N HCl (20 mL) and brine (20 mL) and then dried over magnesium sulfate. The solvent was removed in vacuo and the crude product was purified by silica gel column chromatography (eluting with hexane/EtOAc=8/1) to yield **2a** (92 mg, 91%). R_f=0.47 (EtOAc/hexane=1/8); ^1H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, J=8.8 Hz, 2H), 7.29–7.14 (m, 7H), 2.99–2.94 (m, 4H), 2.57 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.7, 147.3, 140.9, 135.0, 128.6, 128.4, 128.3, 126.0, 37.7, 37.3, 26.4; IR (CH_2Cl_2) 1677, 1604 cm^{-1}; HRMS (CI) calcd for $C_{16}H_{17}O$ $(M+H)^+$ 225.1279, found 225.1286.

3.1.2. 1-(4-Nitrophenyl)-2-phenylethane (2b). Yield=93%; R_f=0.63 (EtOAc/hexane=1/8); ^1H NMR (500 MHz, $CDCl_3$) δ 8.11 (d, J=8.4 Hz, 2H), 7.30–7.26 (m, 4H), 7.22–7.21 (m, 1H), 7.15–7.13 (m, 2H), 3.05–3.02 (m, 2H), 2.97–2.94 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.4, 146.4, 140.4, 129.3, 128.4, 128.3, 126.2, 123.5, 37.6, 37.1; IR (CH_2Cl_2) 1517 cm^{-1}; HRMS (CI) calcd for $C_{14}H_{14}NO_2$ $(M+H)^+$ 228.1024, found 228.1021.

3.1.3. 1-(4-Nitrophenyl)-3-phenylpropane (2d). Yield=94%; R_f=0.72 (EtOAc/hexane=1/8); ^1H NMR (500 MHz, $CDCl_3$) δ 8.12 (d, J=8.6 Hz, 2H), 7.31–7.27 (m, 4H), 7.19–7.16 (m, 3H), 2.75–2.72 (m, 2H), 2.67–2.64 (m, 2H), 1.99–1.97 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.2, 146.3, 141.5, 129.2, 128.4, 128.3, 125.9, 123.6, 35.2, 35.1, 32.4; IR (CH_2Cl_2) 1517, 1452 cm^{-1}; HRMS (CI) calcd for $C_{15}H_{16}NO_2$ $(M+H)^+$ 242.1181, found 242.1181.

3.1.4. Representative procedure B for the cross-coupling reaction of alkylboronic acids with aryl triflates and aryl halides. 1-(4-Acetylphenyl)-3-phenylpropane (2c). To a suspension of 3-phenylpropylboronic acid (**1b**) (82 mg, 0.50 mmol), K_2CO_3 (207 mg, 1.50 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (36 mg, 0.045 mmol), and 4-acetylphenyltriflate (148 mg, 0.55 mmol) in THF (5 mL) was added water (0.5 mL) under an argon atmosphere. The reaction mixture was stirred at reflux temperature for 18 h, then cooled to rt, diluted with water (10 mL), then extracted with ether (20 mL×3). The combined organic layers were washed with 1N HCl (20 mL) and brine (20 mL) and then dried over magnesium sulfate. The solvent was removed in vacuo and the crude product was purified by silica gel column chromatography (eluting with hexane/EtOAc=8/1) to yield **2c** (112 mg, 94%). R_f=0.51 (EtOAc/hexane=1/8); ^1H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J=7.6 Hz, 2H), 7.34–7.23 (m, 7H), 2.75–2.69 (m, 4H), 2.61 (s, 3H), 2.03–2.01 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.5, 147.9, 141.7, 134.9, 128.5, 128.4, 128.3, 128.2, 125.7, 35.2, 35.1, 32.4, 26.3; IR (CH_2Cl_2) 1681, 1605 cm^{-1}; HRMS (CI) calcd for $C_{17}H_{19}O$ $(M+H)^+$ 239.1436, found 239.1425.

3.1.5. 1-(4-Chlorophenyl)-2-phenylethane (2e). Yield=94%; R_f=0.56 (EtOAc/hexane=1/20); ^1H NMR (500 MHz, $CDCl_3$) δ 7.27–7.05 (m, 9H), 2.87 (s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.2, 140.0, 131.6, 129.8, 28.9, 128.4, 128.3, 127.5, 126.2, 126.0, 37.7, 37.2; HRMS (EI) calcd for $C_{14}H_{13}Cl$ (M^+) 216.0706, found 216.0697.

3.1.6. 1-(3-Cyanophenyl)-2-phenylethane (2f). Yield=93%; R_f=0.43 (EtOAc/hexane=1/10); ^1H NMR (500 MHz, $CDCl_3$) δ 7.45–7.11 (m, 9H), 2.93–2.89 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.0, 140.6, 133.2, 132.3, 132.1, 131.2, 129.2, 128.7, 128.5, 128.4, 127.6, 126.7, 119.1, 37.4, 37.3; HRMS (EI) calcd for $C_{15}H_{13}N$ (M^+) 207.1048, found 207.1049.

3.1.7. 1-(3-Trifluoromethylphenyl)-2-phenylethane (2g). Yield=92%; R_f=0.51 (EtOAc/hexane=1/20); ^1H NMR (500 MHz, $CDCl_3$) δ 7.45–7.14 (m, 9H), 2.98–2.91 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.6, 141.1, 131.9, 131.2, 128.8, 128.5, 126.4, 125.2, 124.4, 122.8, 37.7, 37.6; HRMS (EI) calcd for $C_{15}H_{13}F_3$ (M^+) 250.0969, found 250.0969.

3.1.8. 4-Methylacetophenone[36] (2h). Yield=85%; R_f=0.42 (EtOAc/hexane=1/8); ^1H NMR (200 MHz, $CDCl_3$) δ 8.05 (d, J=8 Hz, 2H), 7.45 (d, J=8 Hz, 2H), 2.77 (s, 3H), 2.60 (s, 3H).

3.1.9. 4-Nitrotoluene[36] (2i). Yield=80%; R_f=0.52 (EtOAc/

hexane=1/8); ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.30 (d, J=8.6 Hz, 2H), 7.50 (d, J=8.6 Hz, 2H), 2.65 (s, 3H).

3.1.10. 1-(4-Methoxyphenyl)-2-phenylethane (2j). Yield=15%; R_f=0.36 (ether/hexane=1/20); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.28 (m, 2H), 7.20–7.19 (m, 3H), 7.11 (d, J=8.4 Hz, 2H), 6.84 (d, J=8.5 Hz, 2H), 3.81 (s, 3H), 2.90–2.89 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.8, 141.8, 133.9, 129.3, 128.4, 128.3, 128.2, 125.8, 113.7, 55.2, 38.2, 36.9; IR (CH_2Cl_2) 1583, 1495, 1301 cm^{-1}; HRMS (CI) calcd for $C_{15}H_{17}O$ $(M+H)^+$ 213.1279, found 213.1279.

3.1.11. 1,2-Diphenylethane[36] (2k). Yield=73%; R_f=0.47 (EtOAc/hexane=1/20); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28–7.25 (m, 4H), 7.19–7.16 (m, 6H), 2.91 (s, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.8, 128.4, 128.3, 125.9, 37.9.

3.1.12. 1-(1-Naphthyl)-2-phenylethane (2l). Yield=73%; R_f=0.58 (EtOAc/hexane=1/15); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07–7.20 (m, 12H), 3.35–3.32 (m, 2H), 3.03–3.01 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.9, 137.7, 133.8, 131.7, 129.9, 128.4, 128.3, 128.1, 127.8, 126.7, 126.5, 126.1, 125.9, 125.8, 125.4, 123.6, 37.0, 35.0; HRMS (EI) calcd for $C_{18}H_{16}$ (M^+) 232.1252, found 232.1243.

3.1.13. 1-(2-Methylphenyl)-2-phenylethane (2m). Yield=80%; R_f=0.56 (EtOAc/hexane=1/15); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.28–7.13 (m, 9H), 2.88–2.87 (m, 4H), 2.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.9, 139.9, 135.9, 130.1, 128.8, 128.4, 128.3, 126.1, 125.9, 36.7, 35.4; HRMS (EI) calcd for $C_{15}H_{16}$ (M^+) 196.1252, found 196.1254.

3.1.14. 1-(4-Trifluoromethylphenyl)-2-phenylethane (2n). Yield=67%; R_f=0.52 (ether/hexane=1/8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J=7.8 Hz, 2H), 7.33–7.18 (m, 7H), 3.03–2.95 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.7, 141.0, 128.8, 128.5, 128.4, 127.9, 127.6, 127.5, 126.1, 125.2, 37.6, 37.5; IR (CH_2Cl_2) 1495, 1417 cm^{-1}; HRMS (EI) calcd for $C_{15}H_{13}F_3$ (M^+) 250.0969, found 250.0958.

3.1.15. 1-(4-Benzoylphenyl)-2-phenylethane (2o). Yield=64%; R_f=0.42 (ether/hexane=1/10); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, J=7.6 Hz, 2H), 7.75 (d, J=7.9 Hz, 2H), 7.60–7.57 (m, 1H), 7.50–7.47 (m, 2H), 7.31–7.23 (m, 4H), 7.22–7.19 (m, 3H), 3.05–2.96 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.4, 146.8, 141.1, 137.8, 135.3, 132.2, 130.3, 129.9, 128.4, 128.3, 128.2, 126.1, 37.8, 37.4; IR (CH_2Cl_2) 1654, 1604 cm^{-1}; HRMS (CI) calcd for $C_{21}H_{19}O$ $(M+H)^+$ 287.1436, found 287.1444.

3.1.16. Representative procedure C for the cross-coupling reaction of alkylboronic acids with aryl halides. 1-(2-Trifluoromethyl-4-nitrophenyl)-2-phenylethane (2q). A suspension of 2-phenylethylboronic acid (**1a**) (75 mg, 0.50 mmol), K_2CO_3 (207 mg, 1.50 mmol), $PdCl_2$(dppf)·CH_2Cl_2 (36 mg, 0.045 mmol), and 2-bromo-5-nitrobenzotrifluoride (149 mg, 0.55 mmol) in THF (5 mL) was stirred at reflux temperature for 18 h, then cooled to rt, diluted with water (10 mL), then extracted with ether (20 mL×3). The combined organic layers were washed with 1N HCl (20 mL) and brine (20 mL) and then dried over magnesium sulfate. The solvent was removed in vacuo and the crude product was purified by silica gel column chromatography (eluting with hexane/EtOAc=15/1) to yield **2q** (94 mg, 64%). R_f=0.47 (EtOAc/hexane=1/10); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.31 (d, J=8.4 Hz, 1H), 7.46 (d, J=8.4 Hz, 1H), 7.36–7.35 (m, 2H), 7.29–7.27 (m, 1H), 7.23–7.21 (m, 2H), 3.25–3.22 (m, 2H), 3.00–2.97 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.9, 146.0, 140.1, 132.6, 128.5, 128.4, 126.5, 126.3, 121.7, 37.4, 34.9; IR (CH_2Cl_2) 1595, 1530 cm^{-1}; HRMS (CI) calcd for $C_{15}H_{13}NO_2F_3$ $(M+H)^+$ 296.0898, found 296.0899.

3.1.17. Representative procedure D for the cross-coupling reaction of alkylboronic acids with aryl halides. 1-(4-Nitro-2-pyridyl)-2-phenylethane (2s). A suspension of 2-phenylethylboronic acid (**1a**) (75 mg, 0.50 mmol), K_2CO_3 (207 mg, 1.50 mmol), $Pd(PPh_3)_4$ (58 mg, 0.050 mmol), and 5-nitro-2-chloropyridine (87 mg, 0.55 mmol) in 1,4-dioxane (5 mL) was stirred at reflux temperature for 18 h, then cooled to rt, diluted with water (10 mL), then extracted with ether (20 mL×3). The combined organic layers were washed with 1N HCl (20 mL) and brine (20 mL) and then dried over magnesium sulfate. The solvent was removed in vacuo and the crude product was purified by silica gel column chromatography (eluting with hexane/EtOAc=6/1) to yield **2s** (60 mg, 53%). R_f=0.37 (EtOAc/hexane=1/3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.20 (d, J=8.2 Hz, 1H), 7.35–7.20 (m, 6H), 3.44–3.40 (m, 2H), 3.12–3.09 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.9, 152.7, 146.0, 140.9, 134.1, 132.5, 128.4, 126.2, 122.9, 121.9, 37.7, 34.9; IR (CH_2Cl_2) 2930, 1522, 1351 cm^{-1}; HRMS (CI) calcd for $C_{13}H_{13}N_2O_2$ $(M+H)^+$ 229.0977, found 229.0973.

3.1.18. 1-(3-Nitro-2-pyridyl)-2-phenylethane (2r). Yield=52%; R_f=0.44 (EtOAc/hexane=1/8); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.37 (s, 1H), 8.31 (d, J=8.4 Hz, 1H), 7.28–7.15 (m, 6H), 3.25–3.22 (m, 2H), 3.12–3.09 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.9, 144.8, 142.6, 140.4, 128.5, 128.3, 126.3, 123.1, 40.0, 35.3; IR (CH_2Cl_2) 3064, 1527, 1348 cm^{-1}; HRMS (EI) calcd for $C_{13}H_{12}N_2O_2$ (M^+) 228.0899, found 228.0898.

3.1.19. Representative procedure E for the cross-coupling reaction of alkylboronic acids with aryl halide. 1-(4-Nitrophenyl)-2-phenylethane (2b). A suspension of 2-phenylethylboronic acid (**1a**) (75 mg, 0.50 mmol), K_2CO_3 (207 mg, 1.50 mmol), $PdCl_2$(dppf)·CH_2Cl_2 (36 mg, 0.045 mmol), and 4-bromonitrobenzene (111 mg, 0.55 mmol) in 1,4-dioxane (5 mL) was stirred at reflux temperature for 18 h, then cooled to rt, diluted with water (10 mL), then extracted with ether (20 mL×3). The combined organic layers were washed with 1N HCl (20 mL) and brine (20 mL) and then dried over magnesium sulfate. The solvent was removed in vacuo and the crude product was purified by silica gel column chromatography (eluting with hexane/EtOAc=10/1) to yield **2b** (68 mg, 60%). All spectral data were identical to material prepared by procedure A.

3.1.20. Representative procedure F for the cross-coupling reaction of alkylboronic acids with aryl halide. 1-(4-Cyanophenyl)-2-phenylethane (2p). A suspension of 2-phenylethylboronic acid (**1a**) (75 mg, 0.50 mmol),

Cs_2CO_3 (489 mg, 1.50 mmol), $Pd_2(dba)_3$ (46 mg, 0.05 mmol), dppf (0.075 mmol, 42 mg), and 4-bromobenzonitrile (100 mg, 0.55 mmol) in 1,4-dioxane (5 mL) was stirred at reflux temperature for 18 h, then cooled to rt, diluted with water (10 mL), then extracted with ether (10 mL×3). The combined organic layers were washed with 1N HCl (20 mL) and brine (20 mL) and then dried over magnesium sulfate. The solvent was removed in vacuo and the crude product was purified by silica gel column chromatography (eluting with hexane/EtOAc=6/1) to yield **2p** (75 mg, 72%). R_f=0.65 (EtOAc/hexane=1/3); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53 (d, J=7.6 Hz, 2H), 7.27–7.22 (m, 5H), 7.12 (d, J=6.8 Hz, 2H), 2.97 (d, J=7 Hz, 2H), 2.93 (d, J=7 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.1, 140.5, 132.0, 129.2, 128.4, 128.3, 126.2, 119.0, 109.7, 37.8, 37.1; IR (CH_2Cl_2) 2226 cm^{-1}; HRMS (CI) calcd for $C_{15}H_{14}N$ $(M+H)^+$ 208.1126, found 208.1125.

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