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Palladium-catalyzed cross-coupling reaction of allyl acetates with pinacol aryl- and vinylboronates

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Abstract—Pinacol boronates 2 couple efficiently with allyl acetates 1 in the presence of a palladium catalyst prepared in situ from $PdCl_2$ and TFP to give the coupled products 3 in moderate to good yields under mild conditions. © 2003 Elsevier Science Ltd. All rights reserved.

Aryl- and vinylboronic acid pinacol esters, which are most conveniently prepared by direct borylation of aryl and vinyl halides or triflates,¹ represent an useful alternative to the corresponding boronic acids in the Suzuki-Miyaura cross-coupling reaction.² Their use may be particularly advantageous when the isolation of free boronic acids requires additional protection-deprotection steps or in the presence of functionalities incompatible with the traditional route to boronic acids from Grignard or lithium reagents and trialkyl borates. Compared to the impressive development of the Suzuki-Miyaura coupling, only scanty attention has been paid in the past to the use of organoboron reagents in palladium-catalyzed allylic substitutions³ and, to the best of my knowledge, there are so far no reports on the utilization of pinacol boronates in such reactions.⁴ Recently, Balme et al. have developed a novel catalytic system [PdCl₂(TFP)₂] working guite effectively in cross-coupling reactions of allyl acetates with a variety of arylboronic acids in conjunction with a fluoride source.⁵ Encouraged by this result, I have examined the effectiveness of pinacol boronates in palladium-catalyzed allylation reactions and I report herein that pinacol aryl- and vinylboronates (2) are indeed good substrates for the coupling reaction with allyl acetates (1) (Scheme 1).

Some reaction conditions were briefly explored, using cinnamyl acetate (1a) and 1-naphthylboronate (2a) as



Scheme 1.

model substrates. The results are summarized in Table 1.

Table 1. Reaction of 1a with 2a under various conditions^a

Entry	Catalyst	Base	$Solvent/T \ (^{o}C)$	Yield (%) ^b
1	$Pd(PPh_3)_4$	K ₃ PO ₄	THF/60	46
2	$Pd(PPh_3)_4$	Cs ₂ CO ₃	THF/60	43
3	$Pd(PPh_3)_4$	CsF	THF/60	54
4	Pd ₂ dba ₃	CsF	THF/60	9
5	$Pd(PPh_3)_4$	CsF	DMF/60	69
6	$Pd(PPh_3)_4$	_	THF/60	13
7	$Pd(PPh_3)_4$	_	DMF/60	15
8	PdCl ₂ /2TFP ^c	KF	MeOH/rt	82
9	$PdCl_2/2TFP^c$	_	MeOH/rt	Traces
10	PdCl ₂ /2PPh ₃	KF	MeOH/rt	45
11	PdCl ₂ /dppf ^d	KF	MeOH/rt	Traces

^a All reactions were carried out with 1 mol% of the catalyst, 1.3 equiv. of **2a** and 1.3 equiv. of CsF or 2.6 equiv. of K₃PO₄, Cs₂CO₃ and KF for 4 h (entries 1–7) or 24 h (entries 8–11).

^b Isolated yields.

^c TFP refers to tri-2-furylphosphine.

^d dppf refers to 1,1'-bis(diphenylphosphino)ferrocene.

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Table 2. Palladium-catalyzed cross-coupling of allyl acetates 1 with pinacol boronates $2^{\rm a}$

Entry	Allyl acetate 1	Pinacol boronate	e 2 ^b	Product 3		Yield (%) ^c
1	OAc		2a		3a	82
2	la	A contraction of the second se	2b	Me	3b	91
3	la	, B C CO ₂ Me	2c	CO ₂ Me	3c	84
4	1a		2d	NHCOMe	3d	83
5	1a	Xo, B C, B C, OMe	2e	C C OMe	3e	65
6	1a		2f	BocHN CO2Me	3f	82 ^{d,e}
7	1a	X _o ,	2g		3g	62
8	1a	Aco + + + + + + + + + + + + + + + + + + +	- 2h	Aco	3h	64 ^{d,e,f}
9	// OAc	1b 2d		NHCOMe	3i	88
10	OAc	1c 2d		NHCOMe	3ј	63 ^{dg}
11	OAc	1d 2a		Land South	3k ^h	61 ^d
12	OAc	1e 2a			3k ⁱ	58 ^d

^aAll reactions were carried out in the same manner as described in the text, unless otherwise noted. ^bPinacol boronates **2a-f** and **2g,h** were prepared according to refs. 1b and 1c, respectively. ^cYields of isolated material. ^d 3 mol% of PdCl₂/2TFP were used. ^e1 equiv. of boronate was used. ^fTHF was used to dissolve **2h**. The reaction was carried at 45 °C. ^gReaction time 48 h. ^hE/Z mixture = 83/17. ⁱE/Z mixture = 25/75.

The use of a fluoride salt, as already adopted by Balme, to promote transmetalation⁶ ensuring essentially non basic conditions and thus avoiding some typical problems encountered in Suzuki–Miyaura couplings, was found superior to that of other inorganic bases. The best yields of **3a** were obtained under the optimized conditions developed by Balme for arylboronic acids (entry 8).

The protocol was successfully extended to a variety of allyl acetates and of pinacol aryl- and vinylboronates (Table 2). In a typical procedure (entry 1), a stirred solution of cinnamyl acetate (1a, 176 mg, 1 mmol), PdCl₂ (1.8 mg, 0.01 mmol), TFP (4.6 mg, 0.02 mmol) in MeOH (3 mL) was flushed with N_2 for 10 min at room temperature. Then, KF (151 mg, 2.6 mmol) and a solution of 1-naphthylboronate (2a, 330 mg, 1.3 mmol) in MeOH (2 mL) were added and the mixture was stirred 24 h at room temperature under N₂. The reaction mixture was then diluted with brine and extracted with ether. The organic phase was washed with brine, dried (Na₂SO₄), and evaporated. Chromatography of the residue (289 mg) on silica gel (9 g) using hexane as eluent afforded 199 mg (82%) of (E)-3-(1-naphthyl)-1phenyl-1-propene (3a).

The coupling reactions proceeded generally within 24 h at room temperature and were compatible with both electron-withdrawing and -donating groups. Sterically hindered substrates (2b,h) were also tolerated. Products **3** arose from exclusive attack at the less substituted allyl terminus. No evidence was found in entries 9-12 that the reaction products had suffered some isomerization of the allylic double bond into conjugation with the aromatic moiety. In the case of geranyl (1d) and neryl (1e) acetates, a limited erosion of the stereochemical integrity of the double bond occurred (entries 11, 12). This result, which has precedents in the palladium-catalyzed cross-coupling reactions of allyl substrates with tetraphenylborate anion^{3e} and organotin nucleophiles,⁸ seems to indicate that the transmetalation step of the π -allylpalladium intermediates with the boronate proceeds with a rate comparable to that of the syn/anti-isomerization reaction.

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- 7. Characterization data of coupling products 3. 3a: mp 74-75°C (lit.⁹ mp 74-75°C); IR 3077, 3009, 1597, 1497, 1448, 1396, 1214, 966 cm⁻¹; ¹H NMR δ 3.98 (2H, d, J = 4.8 Hz), 6.41–6.53 (2H, m), 7.15–8.04 (12H, m); ¹³C NMR δ 36.35, 123.78, 125.34, 125.41, 125.70, 125.87, 126.15, 126.85, 128.23, 128.47, 128.63, 131.08, 131.80, 133.65, 135.99, 137.22. 3b: oil; IR 3064, 2927, 1600, 1494, 1448, 967 cm⁻¹; ¹H NMR δ 2.31 (3H, s), 3.50 (2H, d, J = 4.8 Hz), 6.26–6.39 (2H, m), 7.12–7.33 (9H, m); ¹³C NMR & 19.37, 36.77, 125.81, 126.15, 126.77, 128.21, 128.27, 128.95, 129.95, 130.63, 136.11, 137.25, 137.94. 3c: mp 36-37°C; IR 3022, 2949, 1715, 1607, 1438, 1413, 1281, 1113, 964 cm⁻¹; ¹H NMR δ 3.55 (2H, d, J=6.6 Hz), 3.87 (3H, s), 6.28 (1H, td, J=15.6, 6.6 Hz), 6.42 (1H, d, J=15.6 Hz), 7.15–7.33 (7H, m), 7.95 (2H, d, J=8.4 Hz); ¹³C NMR δ 39.17, 51.86, 125.92, 127.07, 127.76, 127.97, 128.30, 128.43, 129.59, 131.57, 136.93, 145.33, 166.71. 3d: mp 130-131°C; IR 3288, 3026, 1656, 1598, 1496, 1409, 1369, 1316, 1266, 1022, 966 cm⁻¹; ¹H NMR δ 2.10 (3H, s), 3.46 (2H, d, J=6.3 Hz), 6.28 (1H, td, J=15.9, 6.3 Hz), 6.40 (1H, d, J=15.9 Hz), 7.13 (2H, d, J=8.5 Hz), 7.16-7.34 (5H, m), 7.42 (2H, d, J=8.5 Hz), 8.02 (1H, br s); ¹³C NMR & 24.29, 38.60, 120.15, 125.86, 126.86, 128.25, 128.82, 128.90, 130.75, 135.82, 135.95, 137.15, 168.50. 3e: mp 33-34°C (lit.3c oil); IR 2929, 2833, 1607, 1510, 1298, 1243, 1178, 1032, 965 cm⁻¹; ¹H NMR δ 3.46 (2H, d, J = 6.3 Hz), 3.75 (3H, s), 6.29 (1H, td, J = 15.9, 6.3 Hz), 6.39 (1H, d, J=15.9 Hz), 6.82 (2H, d, J=8.7 Hz), 7.09-7.33 (7H, m); ¹³C NMR δ 38.37, 55.13, 113.70, 125.86, 126.79, 128.24, 129.35, 129.42, 130.49, 131.91, 137.28, 157.79. 3f: oil; IR 3438, 3010, 2982, 1742, 1709, 1498, 1367, 1166, 966 cm⁻¹; ¹H NMR δ 1.41 (9H, s), 3.02 (1H, dd, J=14.0, 6.1 Hz), 3.09 (1H, dd, J=14.0, 5.7 Hz), 3.51 (2H, d, J = 6.6 Hz), 3.71 (3H, s), 4.57 (1H, m), 4.99 (1H, d)J=8.1 Hz), 6.32 (1H, td, J=15.6, 6.6 Hz), 6.43 (1H, d, J=15.6 Hz), 7.05 (2H, d, J=7.8 Hz), 7.16 (2H, d, J=7.8 Hz), 7.19–7.37 (5H, m); ¹³C NMR δ 28.25, 37.87, 38.88, 52.08, 54.35, 79.76, 125.89, 126.89, 128.26, 128.60, 128.84,

129.19, 130.90, 133.56, 137.18, 138.66, 154.81, 172.05. 3g: oil; IR 2918, 2836, 1600, 1493, 1452, 1435, 967 cm⁻¹; ¹H NMR δ 1.70–2.33 (6H, m), 2.70–2.80 (1H, m), 2.88 (2H, d, J=6.9 Hz), 5.58 (1H, m), 6.23 (1H, td, J=15.6, 6.9 Hz), 6.41 6.41 (1H, d, J=15.6 Hz), 7.15–7.37 (10H, m); $^{13}\mathrm{C}$ NMR δ 29.63, 30.51, 34.06, 40.58, 41.57, 122.09, 126.22, 126.30, 127.13, 127.21, 128.59, 128.73, 128.86, 131.36, 136.67, 137.90, 147.35. 3h: mp 106-109°C; IR 3033, 2939, 2848, 1730, 1451, 1372, 1250, 1031, 962 cm⁻¹; ¹H NMR δ 0.83 (3H, s), 0.97–2.10 (15H, m), 1.06 (3H, s), 2.03 (3H, s), 2.33 (2H, d, J=7.2 Hz), 2.89 (2H, d, J=5.7 Hz), 4.61 (1H, m), 5.38 (2H, m), 6.26 (1H, td, J=15.9, 6.9 Hz), 6.42 (1H, d, J = 15.9 Hz), 7.16–7.37 (5H, m); ¹³C NMR δ 15.74, 19.21, 20.71, 21.37, 27.74, 30.46, 31.13, 31.55, 34.53, 36.79, 36.90, 38.11, 46.43, 50.57, 57.05, 73.80, 122.27, 123.01, 125.78, 126.67, 128.24, 130.67, 137.54, 139.71, 143.52, 153.75, 170.17. 3i: mp 85-88°C (lit.¹⁰ mp 89–92°C); IR 3290, 1663, 1601, 1556, 1511, 1407, 1370, 1321, 1264, 993, 916 cm⁻¹; ¹H NMR δ 2.12 (3H, s), 3.32 (2H, d, J=6.6 Hz), 5.02–5.08 (2H, m), 5.85–5.99 (1H, m), 7.09 (2H, d, J=8.4 Hz), 7.42 (2H, d, J=8.4 Hz), 8.09 (1H, br s); ¹³C NMR δ 24.29, 39.52, 115.53, 120.12, 128.74, 135.76, 135.86, 137.13, 168.56. **3j**; mp 123–125°C; IR 3436, 3009, 2933, 2859, 1686, 1594, 1515, 1411, 1367, 1311, 1246, 1143 cm⁻¹; ¹H NMR δ 1.45–2.08 (6H, m), 2.12 (3H, s), 3.35 (1H, m), 5.66 (1H, dd, J=10.0, 2.0 Hz), 5.87 (1H, m), 7.13 (2H, d, J=8.7 Hz), 7.41 (2H, d, J=8.7 Hz); ¹³C NMR δ 21.02, 24.81, 24.94, 32.50, 41.18, 120.09, 127.89, 128.15, 129.83, 135.65, 142.48, 168.49. **3k**: oil; IR 3048, 2969, 2916, 1597, 1509, 1449, 1396, 1377, 1214, 1108 cm⁻¹; ¹H NMR δ 1.58 (3H, s, *E*-isomer), 1.62 (3H, s, *Z*-isomer), 1.65 (3H, s, *E*-isomer), 1.69 (3H, s, *Z*-isomer), 1.75 (3H, s, *Z*-isomer), 1.78 (3H, s, *E*-isomer), 2.04–2.26 (4H, m), 3.77 (2H, d, *J*=6.6 Hz), 5.08 (1H, m, *E*-isomer), 5.17 (1H, m, *Z*-isomer), 5.39 (1H, t, *J*=6.9 Hz), 7.29–8.01 (7H, m).

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