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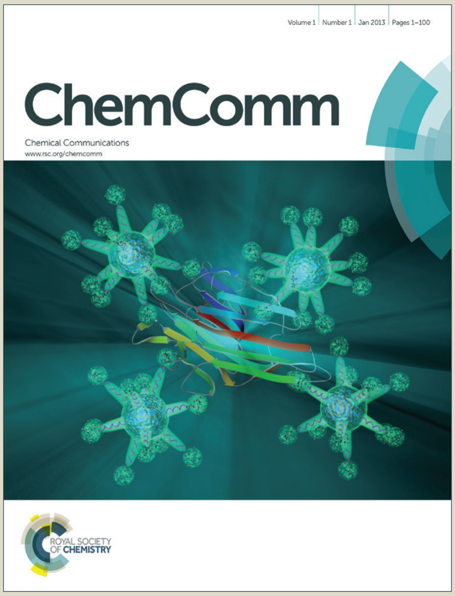

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Palladium NNC-pincer complex: an efficient catalyst for allylic arylation at parts per billion levels

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Allylic arylation of allylic acetates by sodium tetraarylborates in the presence of ppb to ppm (molar) loadings of a palladium NNC-pincer complex catalyst in methanol at 50 °C gave the corresponding arylated products in excellent yields. Total turnover numbers of up to 500,000,000 and turnover frequencies of up to 11,250,000 h^{-1} were achieved.

The development of highly active (high turnover number) transition-metal catalysts is an important topic in organic syntheses and chemical processing, because it permits the use of reduced amounts of toxic or expensive transition metals. Recently, pincer-type transition-metal complexes have received much attention as catalysts in synthetic chemistry because such complexes often exhibit high catalytic activities in various organic transformations.[1] In particular, pincer complexes of palladium have been intensively studied as catalysts.[2] For example, low loadings (molar ppm levels) of palladium pincer complexes efficiently catalyze the Mizoroki–Heck reaction.[3]

The allylic substitution reaction, sometimes known as the Tsuji–Trost reaction, has been recognized as a useful method in the synthesis of natural compounds and pharmaceuticals.[4] While a variety of efficient catalysts for the allylic arylation with arylboron reagents has been developed,[5,6] the reaction often requires a relatively high temperature and a large catalyst loading (1–10 mol%). Therefore, the development of a highly active catalyst for allylic arylation with boron reagents is highly desirable. We recently reported that a self-assembled poly(imidazole–palladium) composite [0.8–40 ppm (molar) Pd] efficiently catalyzes allylic arylation reactions.[7] However, the development of a highly active simple complex as a catalyst for allylic arylation still remains a major challenge. In a continuation of our studies on pincer-palladium complex chemistry,[8,9] we found that extremely small amounts (1 ppb to 1 ppm molar) of the palladium NNC-pincer complex **1**[10,11] efficiently catalyze the allylic arylation of aromatic and aliphatic allylic acetates by sodium tetraarylborates in methanol.

Initially, we examined the allylic arylation of cinnamyl acetate (**2a**) with sodium tetraphenylborate (**3a**) in the presence of 0.1 mol% of the palladium NNC-pincer complex **1** (Table 1, entry 1). The reaction was completed within 1 hour and gave 1,1'-[(1*E*)-prop-1-ene-1,3-diyl]dibenzene (**4aa**) in 91% isolated yield. Next, we tried the reaction with 1 mol ppm of complex **1**. Fortunately, we found that the reaction of acetate **2a** with borate **3a** in the presence of 1 mol ppm of

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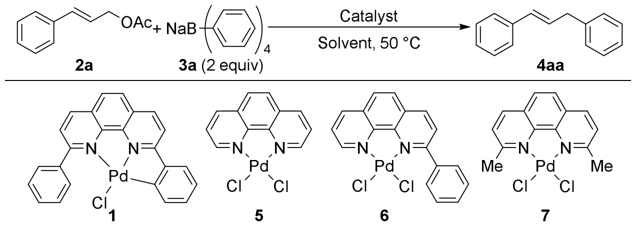
Table 1 The allylic arylation of cinnamyl acetate (**2a**) with sodium tetraphenylborate (**3a**) in the presence of palladium NNC-pincer complex **1**

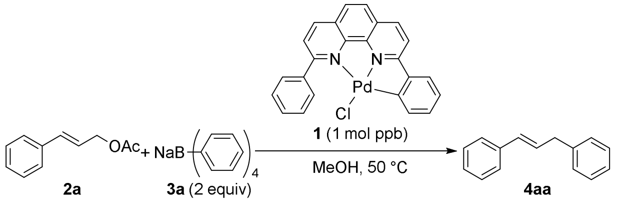


Entry	Catalyst	Catalyst concentration	Solvent	Time (h)	Yield[a] (%)
1[b]	**1**	0.1 mol%	MeOH	1	91
2[c]	**1**	1 mol ppm	MeOH	24	87
3[d]	**1**	0.1 mol%	MeOH	15	57
4[c]	**1**	none	MeOH	24	nr[e]
5[c]	**1**	1 mol ppm	THF	24	76
6[c]	**1**	1 mol ppm	H_2O	24	69
7[c]	**1**	1 mol ppm	DMF	24	nr[e]
8[c]	**1**	1 mol ppm	TCE	24	1
9[c]	**1**	1 mol ppm	toluene	24	nr
10[f]	**5**	1 mol ppm	MeOH	24	16
11[f]	**6**	1 mol ppm	MeOH	24	45
12[f]	**7**	1 mol ppm	MeOH	24	56

[a] Isolated yield; [b] *Reaction conditions*: **1** (3.0×10^{-4} mmol), **2a** (0.3 mmol), **3a** (0.6 mmol), MeOH (1 mL), 50 °C, 1 h; [c] *Reaction conditions*: **1** (1.0×10^{-5} mmol), **2a** (10 mmol), **3a** (20 mmol), solvent (10 mL), 50 °C, 24 h; [d] *Reaction conditions*: **1** (3.0×10^{-4} mmol), **2a** (0.3 mmol), phenylborpnic acid (0.6 mmol), KF (0.75 mmol), MeOH (1 mL), reflux, 15 h; [e] nr = no reaction; [f] *Reaction conditions*: **5**, **6** or **7** (1.0×10^{-5} mmol), **2a** (10 mmol), **3a** (20 mmol), MeOH (10 mL), 50 °C, 24 h.

1 at 50 °C for 24 hours in methanol gave the desired arylated product **4aa** in 87% isolated yield (entry 2). In this reaction, the turnover number (TON) was 870,000 and the turnover frequency (TOF) was 36,250 h^{-1}. When phenylboronic acid was used as a coupling nucleophile, the reaction gave 57% yield of **4aa** even with 0.1 mol% of the catalyst **1** after 15 hours (entry 3). No reaction occurred in the absence of complex **1** (entry 4). We then investigated the effect of the solvent on the reaction. The reaction proceeded smoothly in tetrahydrofuran (THF) or water to give product **4aa** in similar yields (entries 5 and 6). In contrast, no reaction occurred in *N,N*-dimethylformamide (DMF), 1,1,2,2-tetrachloroethane (TCE), or toluene (entries 7–9). The palladium complexes **5**, **6** and **7**, which lack the NNC-pincer structure exhibited lower catalytic activity to give the desired product **4aa** in 16, 45, and 56% yield, respectively (entries 10–12).

Next, we attempted to perform an allylic arylation with an even lower loading of complex **1**. The reaction of cinnamyl acetate (**2a**) with sodium tetraphenylborate (**3a**) in the presence of 1 mol ppb of complex **1** in methanol at 50 °C for 24 h gave the desired product **4aa** in 27% yield (Scheme 1). When the reaction time was prolonged to 96 h, the yield of **4aa** increased to 50%. In this case, the turnover number increased to 500,000,000 and the turnover frequency was 11,250,000 h^{-1}.



24 h: 27% yield (TON = 270,000,000, TOF = 11,250,000 h^{-1})
96 h: 50% yield (TON = 500,000,000, TOF = 5,210,000 h^{-1})

Scheme 1 Allylic arylation of acetate **2a** with borate **3a** catalyzed by 1 mol ppb of complex **1**. *Reaction conditions*: **1** (1.0×10^{-8} mmol), **2a** (10 mmol), **3a** (20 mmol), MeOH (10 mL). The yields refer to isolated products.

The catalytic activities of the phenanthroline palladium(II) complexes are affected by the steric hinderance around palladium. Thus, the activities of complexes **6** (TON = 450,000) and **7** (TON = 560,000) were superior to that of complex **5** (TON = 160,000) (entries 10–12, Table 1). However, a noteworthy advance in catalytic activity was achieved with the NNC-pincer backbone. Thus, the turnover number of palladium increased by triple digits with the NNC-pincer complex **1** to realize 270,000,000 of TON within 24 hours (Scheme 1).

We then examined the allylic arylation of various allylic acetates with sodium tetraarylborates in the presence of complex **1** (1 mol ppm) (Scheme 2). The reaction of sodium tetraphenylborate (**3a**) with cinnamyl acetates bearing electron-donating or electron-withdrawing substituents **2b**–**2i** proceeded smoothly to give the corresponding arylated products **4ba**–**4ia** in yields of 77–95%. The reaction of (2*E*)-3-(2-naphthyl)prop-2-en-1-yl acetate (**2j**) gave 2-[(1*E*)-3-phenylprop-1-en-1-yl]naphthalene (**4ja**) in 99% yield. Sterically hindered 2-methyl- and 2-methoxycinnamyl acetates (**2k** and **2l**, respectively) gave 1-methoxy-2-[(1*E*)-3-phenylprop-1-en-1-yl]benzene (**4ka**) and 1-methyl-3-[(1*E*)-3-phenylprop-1-en-1-yl]benzene (**4la**) in 93 and 83% yield, respectively. Allylic arylation of cinnamyl acetate (**2a**) with sodium tetraarylborates **3b**–**3d** also proceeded in the presence of complex **1** to give the corresponding arylated products **4ab**, **4ac**, and **4ad**, respectively, in yields of 59–84%. Complex **1** also catalyzed the reaction of less-reactive aliphatic 2-alkenyl acetates with sodium tetraphenylborate (**3a**). The reactions of hex-2-enyl acetate (**2m**), 3-methyl-2-buten-1-yl acetate (**2n**), cyclohex-2-en-1-yl acetate (**2o**), neryl acetate (**2p**), or geranyl acetate (**2q**) in the presence of complex **1** (1 mol ppm) gave the corresponding arylated products **4ma**–**4qa** in yields of 54–78%. The secondary allylic acetates **2r** and **2s** also underwent the reaction to give the phenylated products **4ra** and **4sa** in 74 and 58% yield, respectively. However, the reactions of (2*E*)-3-(2-thienyl)prop-2-en-1-yl acetate (**2r**) and (2*E*)-3-pyridin-3-ylprop-2-en-1-yl acetate (**2s**) were sluggish, suggesting that strongly coordinating substrates inhibit allylic arylations catalyzed by complex **1**.

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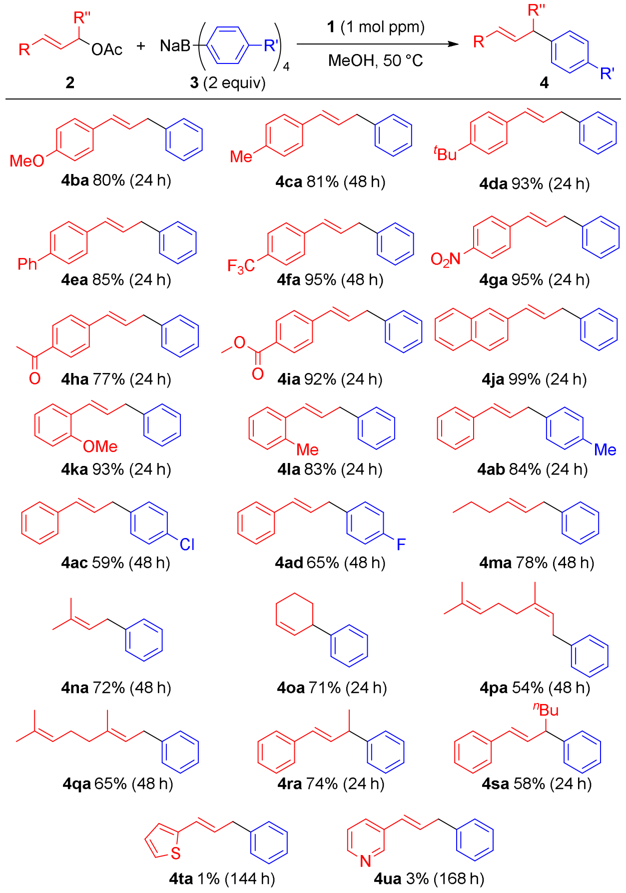
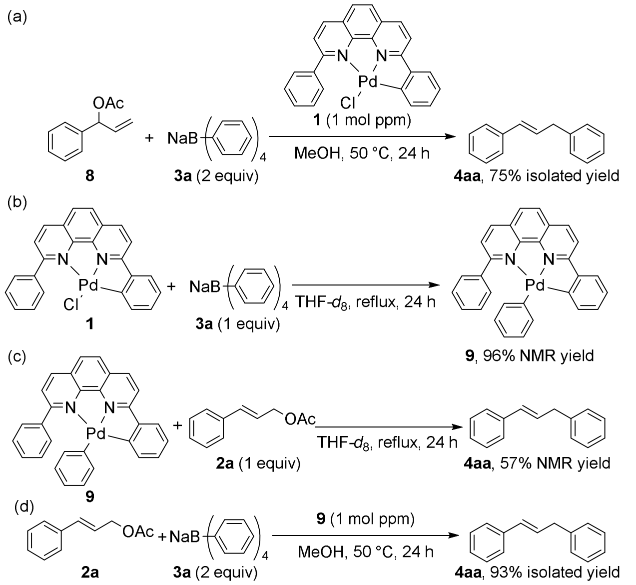


Scheme 2 Allylic arylations of various allylic acetates with sodium tetraarylborates in the presence of palladium NNC-pincer complex **1**. *Reaction conditions:* **1** (1.0×10^{-5} mmol), **2** (10 mmol), **3** (20 mmol), MeOH (10 mL), 50 °C. The yields refer to isolated products.

We then performed several experiments in an attempt to identify the reaction pathway for the allylic arylation reaction catalyzed by complex **1** (Scheme 3). The reaction of the branched acetate **8** with borate **3a** in the presence of complex **1** gave alkene **4aa** in 75% yield (Scheme 3a). This result suggested that a π-allyl Pd intermediate is generated in the catalytic cycle. Treatment of complex **1** with one equivalent of borate **3a** gave the phenylated complex **9** in 96% yield (NMR; Scheme 3b).[12] The reaction of complex **9** with acetate **2a** gave alkene **4aa** in 56% yield (NMR; Scheme 3c). We also examined the reaction of acetate **2a** with borate **3a** in the presence of 1 mol ppm of complex **9**. The desired arylated product **4aa** was obtained in 93% isolated yield (Scheme 3d). These results indicated that complex **9** is a possible intermediate in the allylic arylation.



Scheme 3 Mechanistic investigations.

In summary, we found that the allylic arylation of various allylic substrates with sodium tetraarylborates in the presence of palladium NNC-pincer complex **1** at loadings of the order of ppb to ppm (molar) proceeded smoothly under mild conditions to give the desired arylated products in good-to-excellent yields. Turnover numbers of up to 500,000,000 and turnover frequencies of up to 11,250,000 h^{-1} were achieved.

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Notes and references

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