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Novel bis(oxazole) pincer ligands for catalysis: Application in Suzuki-Miyaura cross coupling reactions under aerobic conditions

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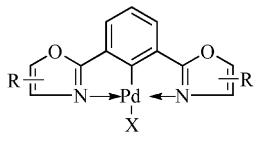
Abstract

Introducing bis(oxazole) ligands to catalysis: novel bis(oxazole) ligands could be readily synthesized from isophthaloyl dichlorides and ethyl glycinate hydrochlorides or 6-aminoacetophenone hydrochloride. Their corresponding pincer palladium complexes proved to be extremely robust catalysts for Suzuki-Miyaura cross coupling reactions, allowing the synthesis of biaryls under aerobic conditions with turn over numbers of up to 790,000 and turn over frequencies of up to 49,000 h^{-1}.

Keywords: Bis(oxazoles); Pincer ligands; Suzuki-Miyaura cross coupling; Palladium; Biaryls

1. Introduction

The oxazoline moiety has proved to be an excellent donor for metals, and especially bis(oxazolines) are recognized to be superior ligands for catalysis [1]. One drawback of oxazolines is their lability towards hydrolysis, especially at higher reaction temperatures and under acidic conditions. Based on our own interest in the development of bis(oxazoline) [2] and azabis(oxazoline) [3] ligands for catalysis, we wanted to explore bis(oxazoles) as an alternative, more stable ligand framework to form metal complexes, for which to the best of our knowledge no applications in catalysis have been reported [4]. As a starting point for bis(oxazoles) we chose pincer ligands of the NCN type since it was expected that especially stable palladium complexes **1** should be formed that would allow their detailed characterization.



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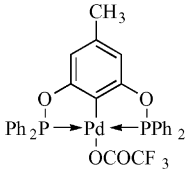

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Moreover, as a first benchmark application of these complexes in Suzuki-Miyaura cross coupling reactions were envisioned [5], for which PCP–palladium complexes such as **2** have been proved to give excellent results [6].

2. Experimental

2.1. Chemicals

Commercially available reagents were used as received. DMF, $ClCH_2CH_2Cl$ and CH_2Cl_2 were distilled over P_2O_5 and stored under N_2 over molecular sieves 3 Å. THF, 1,4-dioxane and benzene were dried with Na/benzophenone and stored over Na-wire under N_2. EtOAc, Et_2O, CH_2Cl_2 and hexanes for chromatographic separations were distilled before use. For column chromatography silica gel Geduran 60 (Merck, 0.063–0.200 mm) was used. TLC-analysis was done on silica gel 60 F_{254} (Merck) coated on aluminum sheets.

2.2. Synthesis of bis(oxazole) ligands

2.2.1. Bis(oxazole) **5a** [7a]

Isophthaloyl dichloride **4a** (1.22 g, 6 mmol) and ethyl glycinate hydrochloride (2.51 g, 18 mmol) were suspended in 40 mL of dry CH_2Cl_2, and Et_3N (8.4 mL, 60 mmol) was added dropwise at 0 °C. After being stirred for 30 h with gradual warming to room temperature, the resultant mixture was diluted with

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200 mL of EtOAc and washed with water (2× 50 mL), the water phase was extracted with 150 mL of EtOAc. The combined organic phase was washed with 10% aqueous HCl, water, and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and then filtered and concentrated under reduced pressure to yield *N*,*N*′-bis(2-oxo-2-ethoxyethyl)isophthalamide (**A**) (2.0 g, 99% yield) as a colorless oil which slowly solidified. The compound could be used in the next step without purification. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.20 (t, J = 1.6 Hz, 1H), 7.92 (dd, J = 1.8, 7.8 Hz, 2H), 7.46 (t, J = 7.7 Hz, 1H), 7.09 (t, J = 5.1 Hz, 2H), 4.26 (q, J = 7.1 Hz, 4H), 4.23 (d, J = 5.2 Hz, 4H), 1.32 (t, J = 7.1 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.2, 166.7, 133.9, 130.5, 129.0, 125.4, 61.8, 41.9, and 14.2. A mixture of **B** (338 mg, 1 mmol) and P_2O_5 (2.8 g, 20 mmol) in 40 mL of dry $ClCH_2CH_2Cl$ was stirred for 14 h at 90 °C. The reaction mixture was cooled to room temperature, diluted with 30 mL of Et_2O, and then carefully neutralized with 10% cold KOH aqueous solution (*ca.* 35 mL) followed by extraction with EtOAc (three portions of 50 mL). The combined organic phase was washed with water and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and then filtered and concentrated to dryness. The crude product was purified by column chromatography (silica, hexanes:EtOAc 1:1 as eluent) to afford 39 mg of **5a** as a pale white solid. Yield 13%. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.42 (t, J = 1.5 Hz, 1H), 7.92 (dd, J = 1.8, 7.8 Hz, 2H), 7.46 (t, J = 7.8 Hz, 1H), 6.22 (s, 2H), 4.19 (q, J = 7.0 Hz, 4H), 1.45 (t, J = 7.1 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.9, 151.9, 129.2, 128.2, 126.1, 122.1, 101.1, 68.2, 14.6.

2.2.2. *Bis(oxazole)* ***5b***

2-Bromoisophthaloyl dichloride **4b** [7b] (1.73 g, 6 mmol) and ethyl glycinate hydrochloride (2.51 g, 18 mmol) were suspended in 40 mL of dry CH_2Cl_2, and Et_3N (8.4 mL, 60 mmol) was added dropwise at 0 °C. After being stirred for 30 h with gradual warming to room temperature, the resultant mixture was concentrated, diluted with 70 mL of H_2O, and then extracted with CH_2Cl_2 (four portions of 150 mL each). The combined organic phase was washed with 10% aqueous HCl, water, and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and then filtered and concentrated under reduced pressure to yield 2-bromo-*N*,*N*′-bis(2-oxo-2-ethoxyethyl)isophthalamide (**B**) (2.10 g, 84% yield) as a white solid. The compound could be used in the next step without purification. mp 191–192 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54 (dd, J = 7.1, 8.0 Hz, 2H), 7.42 (dd, J = 6.9, 8.2 Hz, 1H), 6.48 (t, J = 4.8 Hz, 2H), 4.27 (q, J = 7.1 Hz, 4H), 4.25 (d, J = 5.0 Hz, 4H), 1.32 (t, J = 7.1 Hz, 6H). A mixture of **B** (1.66 g, 4 mmol) and P_2O_5 (7.5 g, 52.8 mmol) in 80 mL of dry $ClCH_2CH_2Cl$ was heated for 30 min at 60 °C, and then stirred for 14 h at 90 °C. The reaction mixture was cooled to room temperature, diluted with 50 mL of Et_2O, and then carefully neutralized with 10% cold NaOH (*ca.* 55 mL) followed by extraction with EtOAc (3× 150 mL each). The combined organic phase was washed with water and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and then filtered and concentrated. The crude product was purified by column chromatography (silica, hexanes:EtOAc 1:1 as eluent) to afford **5b** (880 mg, 58% yield) as a light yellow solid. mp 56–57 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.80 (d, J = 8.0 Hz, 2H), 7.43 (t, J = 7.8 Hz, 1H), 6.31 (s, 2H), 4.22 (q, J = 7.1 Hz, 4H), 1.47 (t, J = 7.1 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.1, 150.9, 132.1, 130.9, 127.3, 120.0, 100.9, 68.3, 14.6. MS (EI-MS): m/z (%) = 380.1 (56), 378.1 (57) [M^+], 296.1 (98), 294.0 (100), 268.0 (44), 266.0 (46). Elemental analysis for $C_{16}H_{15}BrN_2O_4$: found C 50.99, H 4.21, N 7.14, Br 20.51; calcd. C 50.68, H 3.99, N 7.39, Br 21.07.

2.2.3. *Bis(oxazole)* ***5c***

To a stirred mixture of isophthaloyl dichloride (**4a**) (1.01 g, 5.0 mmol, 1.0 equiv.) in 12 mL of dry pyridine was added in portions α-aminoacetophenone hydrochloride (1.88 g, 11 mmol, 2.2 equiv.). The reaction was refluxed for 30 min. Then the mixture was allowed to cool and diluted with water. The precipitate was filtered and dissolved in hot ethyl acetate. The organic solution was concentrated to a smaller volume and diethyl ether was added. White to beige product commences to crystallize out. Filtration afforded the crude product (0.99 g, 2.47 mmol, 49%), which was used without further purification. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 9.02 (t, 2H, J = 5.5 Hz), 8.48–8.42 (m, 1H), 8.12–8.00 (m, 6H), 7.74–7.52 (m, 7H), 4.83 (d, 4H, J = 5.5 Hz); ^{13}C NMR (75.5 MHz, DMSO-d_6): δ = 195.1, 166.0, 135.0, 134.1, 133.5, 129.9, 128.8, 128.5, 127.8, 126.4, 46.4; MS (PI-EIMS): m/z (%) = 400.2 (14) [M^+], 295.2 (11) [$M^+ - PhCO$], 266.1 (84) [$M^+ - PhCOCH_2NH$], 105.1 (100) [$PhCO^+$], 77.1 (25) [Ph^+]. A mixture of *N*,*N*′-bis-(2-oxo-2-phenyl-ethyl)isophthalamide (1.03 g, 2.57 mmol, 1.0 equiv.) in 40 mL phosphorus oxychloride was refluxed for 16 h. Most of the phosphorus oxychloride was distilled in vacuum into a cold trap from the reaction mixture, and the residue was slowly added to water contained in a 250 mL beaker. The solid was filtered, washed with water and dried (crude product). Recrystallization from pyridine afforded 0.49 g (1.34 mmol, 52%) of **5c** as a white to beige solid. mp 177 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.85–8.79 (m, 1H), 8.21 (dd, 2H, J = 7.8, 1.6 Hz), 7.81–7.74 (m, 4H), 7.61 (t, 1H, J = 7.8 Hz), 7.55–7.43 (m, 6H), 7.41–7.33 (m, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 160.4, 151.8, 129.5, 129.0, 128.7, 128.2, 128.0, 127.8, 124.4, 123.8, 123.5; IR (KBr): 3110, 3060, 1600, 1580, 1565, 1530, 1480, 1470, 1445, 1420, 1135, 1075, 1060, 1030, 965, 950, 940, 910, 860, 825, 800, 760, 710, 680 cm^{-1}; MS (PI-EIMS): m/z (%) = 364.2 (100) [M^+]; $C_{24}H_{16}N_2O_2$ (364.40): calcd. C 79.11, H 4.43, N 7.69; found C 78.42, H 3.77, N 7.49.

2.2.4. *Bis(oxazole)* ***5d***

To a stirred mixture of 2-bromo-1,3-benzenedicarbonyl dichloride (**4b**) (1.50 g, 5.32 mmol, 1.0 equiv.) in 15 mL of dry pyridine was added in portions α-aminoacetophenone hydrochloride (2.00 g, 11.71 mmol, 2.2 equiv.). The reaction was refluxed for 15 min—the mixture got red, then yellow. The reaction was allowed to cool and diluted with water. The resulting precipitate was filtered, washed with diethyl ether and dried. This crude product was stirred in 20 mL of ethyl acetate. Filtration of the cold (0 °C) mixture afforded the product as beige solid (1.76 g, 3.67 mmol, 69%). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.87 (t, 2H, J = 5.6 Hz), 8.10–8.01 (m, 4H), 7.74–7.65 (m, 2H), 7.63–7.44 (m, 7H), 4.78 (d, 4H,

$J = 5.6$ Hz); MS (ESI, CH_2Cl_2/MeOH + 10 mmol/L NH_4OAc): m/z (%) = 498.0 (100) [$M + NH_4^+$], 481.0 (55) [M^+], 385.0 (25), 377.8 (22), 360.8 (12). A mixture of 2-bromo-*N*,*N*′-bis-(2-oxo-2-phenyl-ethyl)isophthalamide (0.239 g, 0.50 mmol, 1.0 equiv.) and 0.860 g (3.00 mmol, 6.0 equiv.) of phosphorus oxybromide was heated to 140 °C for 2 h. After the reaction was allowed to cool to room temperature, water was added slowly to the resulting slurry and the product was extracted twice with ethyl acetate. The organic fraction was washed with brine, dried ($MgSO_4$) and concentrated in vacuum (0.218 g crude material). Column chromatography (SiO_2, 5 cm × 8 cm, ethyl acetate) afforded 0.191 g, which were recrystallized from 3 mL ethyl acetate to get 100 mg (0.23 mmol, 45%). R_f (SiO_2, EtOAc) = 0.60 (UV); mp 143 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.03$ (d, 2H, $J = 7.7$ Hz), 7.82–7.69 (m, 4H), 7.62–7.32 (m, 9H); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 159.7, 152.2, 133.1, 131.1, 129.0, 128.8, 127.8, 127.5, 124.5, 123.2, 120.6$; IR (KBr): 3113, 3062, 3030, 2375, 1951, 1564, 1528, 1507, 1483, 1450, 1396, 1355, 1319, 1152, 1113, 1063, 1026, 970, 945, 909, 851, 804, 760, 722, 686 cm^{-1}; MS (PI-EIMS): m/z (%) = 442.1 (100) [M^+], 364.2 (20) [MH$^+$ − Br], 308.2 (40), 190.2 (16), 105.1 (24), 77.1 (22); $C_{24}H_{15}BrN_2O_2$ (443.29): calcd. C 65.03, H 3.41, N 6.32; found C 65.02, H 3.46, N 6.32.

2.3. Synthesis of palladium–bis(oxazole) complex 8

Under a N_2 atmosphere, a 50 mL Schlenk flask was charged with **5b** (373 mg, 0.65 mmol), (246 mg, 0.65 mmol) $Pd(dba)_2$, and 30 mL of dry benzene. The reaction mixture was heated to reflux until the purple color faded (*ca.* 30 min, from purple to dark green or yellow), then cooled to room temperature and stirred for further 2 h, followed by filtration to remove the precipitate. To the filtrate was slowly added hexane (*ca.* 40 mL) to precipitate the product **8**. Crystallization from CH_2Cl_2/EtOAc afforded **8** (277 mg, 87% yield) as yellow needles. Crystals of **8** suitable for X-ray diffraction analysis were grown with slow diffusion of EtOAc into a concentrated CH_2Cl_2/EtOAc (5:1, v/v) solution of **8**. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.21$–7.09 (m, 3H), 6.55 (s, 2H), 4.23 (q, $J = 7.0$ Hz, 4H), 1.48 (t, $J = 7.0$ Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 164.6, 159.9, 158.7, 130.2, 125.0, 121.6, 100.5, 69.6, 14.5$. MS (FI-FDMS): m/z (%) = 969.7 (3) [2M^+], 890.6 (92) [2M^+ − HBr], 485.9 (100) [M^+], 405.1 (5) [M^+ − HBr]. Element analysis: found C 39.65, H 3.15, N 5.75, Br, 16.46; calcd. C 39.57, H 3.11, N 5.77, Br, 16.45.

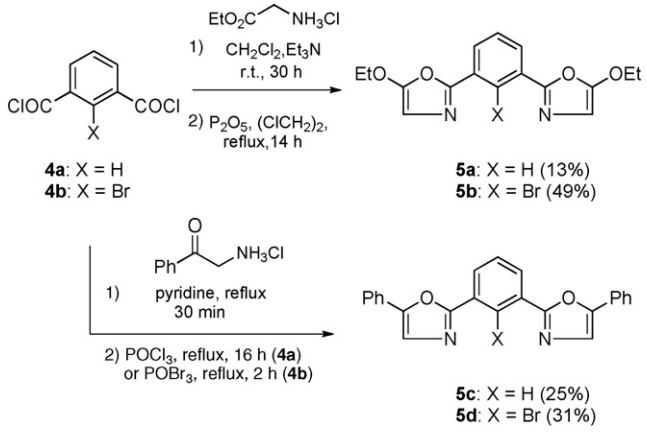
2.4. Suzuki-Miyaura coupling reactions: general procedure (under aerobic atmosphere in either N_2-degassed solvent or normal analytic solvent)

Phenylboronic acid (1.5 mmol unless otherwise indicated), aryl bromide (1.0 mmol), anhydrous K_2CO_3 (3.0 mmol), 1,4-dioxane (5.0 mL, N_2-degassed or normal analytic reagent) and the indicated amount of catalyst **8** were charged into a 10 mL round flask with a condenser. Note that (1) the liquid aryl bromides were added after the addition of solvent and (2) if the amount of **8** was less than 1.0 mg, appropriate volumes of a solution of **8** (1.0×10^{-4} mol/L Pd in analytic grade 1,4-dioxane) was used. The total volume of solvent was 5.0 mL in each reaction. The mixture was heated at reflux temperature for 16 h, diluted with 10 mL of distilled water, and extracted with EtOAc (2× 30 mL). The combined organic phase was washed with distilled water and saturated aqueous NaCl, dried over anhydrous $MgSO_4$ and then filtered and concentrated. The crude product was purified by column chromatography (silica, hexanes or hexanes/EtOAc mixture as eluent).

3. Results and discussion

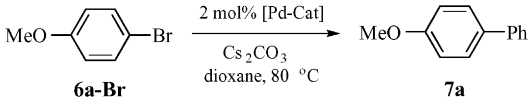
Bis(oxazole) ligands could be readily synthesized in moderate yields from isophthaloyl dichlorides **4** and ethyl glycinate hydrochloride (**5a**,**b**) or α-aminoacetophenone hydrochloride (**5c**,**d**) (Scheme 1). In this sequence, the last cyclization step is low yielding, which is in part due to the low solubility of some of the ligands. Nevertheless, all bis(oxazole) ligands could be obtained in high purity by column chromatography and/or recrystallization.

As a test for the new ligands we followed a report from Tao and Boykin who showed the bis(oxazoline) **3** to be an effective



Scheme 1. Synthesis of bis(oxazoles) **5**.

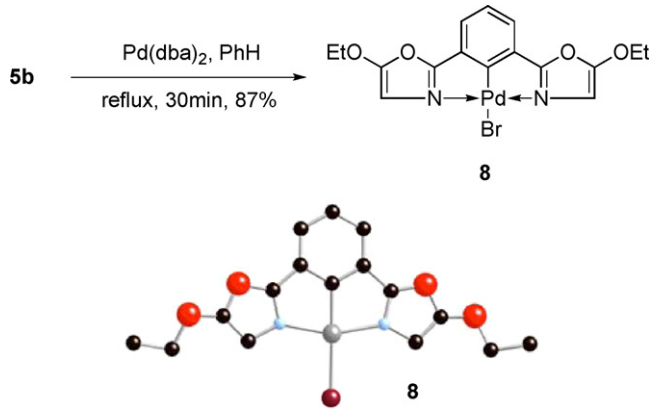
Table 1
Palladium-catalyzed cross coupling of 4-bromoanisole (**6a**-Br) and phenylboronic acid[a]



6a-Br **7a**

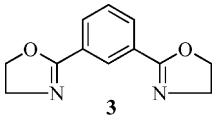
Entry	Pd-source	Ligand	Yield (%)
1[b]	$Pd(OAc)_2$	**3**	96
2	$Pd(OAc)_2$	**5a**	18
3	$Pd(dba)_2$	**5a**	10
4	$Pd(OAc)_2$	**5b**	45
5	$Pd(dba)_2$	**5b**	35
6[c]	$Pd(OAc)_2$	–	22

[a] Conditions: 4-bromoanisole (1.0 mmol), phenylboronic acid (1.5 mmol), $Pd(OAc)_2$ or $Pd(dba)_2$ (2.0 mol%), **6a** or **6b** (2.0 mol%), Cs_2CO_3 (2.0 mmol), 1,4-dioxane (4 mL), 80 °C, 4 h.
[b] Taken from Ref. [8].
[c] *cf.* also Ref. [11].



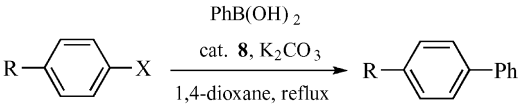
Scheme 2. Synthesis of the palladium–bis(oxazole) pincer complex **8**.

ligand for the Suzuki-Miyaura coupling, giving high yields with a variety of aryl halides and boronic acids at a catalyst loading of 2 mol% [8]. The catalyst was formed *in situ* by mixing **3** with $Pd(OAc)_2$, and it was speculated that a bis(oxazoline) palladacycle could have formed, representing the catalytically active species [9].



In the presence of $Pd(OAc)_2$ or $Pd(dba)_2$ under conditions that have been successful with ligand **3** [8] in the Suzuki-Miyaura coupling (Table 1, entry 1), both, **5a** and **5b** [10] gave disappointing results (Table 1, entries 2–5), hardly exceeding the

Table 2
Suzuki-Miyaura coupling of phenylboronic acid with 4-sustituted halobenzenes[a]

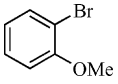
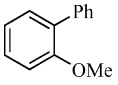
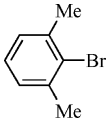
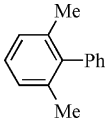
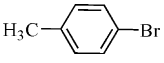
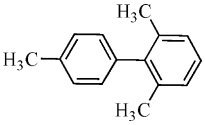
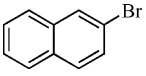
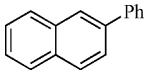
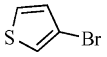
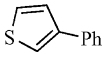
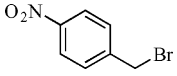
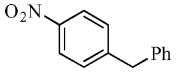


6-X **7**

Entry	**6**-X	R	**9** (mol%)	**8**	Yield (%)	TON
1[b]	**6a**-Br	OMe	0.2	**7a**	≥99	495
2[c]	**6b**-I	Me	0.2	**7b**	≥99	495
3[b]	**6b**-I	Me	0.0001	**7b**	79	7.90×10^5
4[c]	**6b**-Br	Me	0.002	**7b**	≥99	4.95×10^4
5[b]	**6b**-Br	Me	0.0002	**7b**	51	2.55×10^5
6[c]	**6b**-Br	Me	0	**7b**	0	–
7[b]	**6c**-Br	NMe_2	0.01	**7c**	95	9.5×10^3
8[c,d]	**6d**-Br	Ac	0.2	**7d**	90	450
9[e]	**6d**-Br	Ac	0.2	**7d**	≥99	495
10[c]	**6d**-Cl	Ac	0.2	**7d**	7	35
11[b,f]	**6d**-Cl	Ac	4	**7d**	31	8

[a] Phenylboronic acid (1.5 mmol), aryl halide (1.0 mmol), **8**, K_2CO_3 (3.0 mmol), 1,4-dioxane (5.0 mL), 16 h reflux. Isolated yields are given in all cases; TON: turnover number, ratio of yield to catalyst amount.
[b] Reaction performed under aerobic atmosphere with analytical grade solvent.
[c] Reaction performed under aerobic atmosphere with N_2-degassed solvent.
[d] Refluxing time was 10 h.
[e] Reaction performed under nitrogen atmosphere.
[f] Two millimoles of phenylboronic acid were used and reaction refluxed for 20 h.

Table 3
Suzuki-Miyaura coupling of arylboronic acid with aryl, heteroaryl and benzyl bromides[a]

Entry	Ar–Br	**8** (mol%)	Product	Yield[b] (%)	TON
1		0.01		84	8.4×10^3
2		0.01		45	4.5×10^3
3		0.1		30	300
4		0.01		94	9.4×10^3
5		0.2		55	275
6		0.01		10[c]	1.0×10^3
7		0.01		≤2[c]	–
8		0.01		79	7.9×10^3

[a] 1.5 mmol phenylboronic acid, 1.0 mmol aryl halide, indicated amount of catalyst **8**, 3.0 mmol K_2CO_3, and 1,4-dioxane (5 mL); all reactions were run open to air with analytical grade solvent that was used as received.
[b] Isolated yields.
[c] Determined by NMR.

performance of $Pd(OAc)_2$ in the absence of any ligand (Table 1, entry 6) [11]. Obviously, under these conditions a palladium pincer complex was not formed (*cf.* below). We therefore tried to preform the anticipated palladium pincer complexes: while **5a** and **5c** in the presence of $Pd(dba)_2$ did not undergo a cyclometallation, **5b** cleanly gave rise to **8**, which could be isolated in 87% yield as a crystalline compound and futhermore stored open to air for several weeks without apparent degradation. The X-ray structure analysis of **8** clearly showed the successful formation of a pincer complex (Pd–N = 2.06 Å, Pd–C = 1.96 Å) [12] (Scheme 2).

Likewise, **6d** could be transformed into the palladium complex corresponding to **8**, which proved however, to be extremely insoluble in organic solvents, prohibiting its further evaluation.

Gratifyingly, we found that **8** is able to promote the Suzuki-Miyaura coupling (Tables 2 and 3) choosing K_2CO_3 as base, while with CsF, Cs_2CO_3 or K_3PO_4 slightly inferior results were obtained. While only moderate catalytic activity was observed for the coupling of aryl chlorides, the apparent robustness of **8** allowed the coupling of aryl bromides and iodides, both, electron rich as well as electron deficient ones, with turn over number of up to 790,000 and, most notably, without the exclusion of oxygen from the reaction setup.

To further explore the scope and limitation of palladium bis(oxazole) **8**, a number of additional substrates were tested under aerobic conditions. Sterically hindered arenes underwent coupling with acceptable turn over numbers. Heteroarenes turned out to be less suitable substrates for the coupling reactions, probably due to the interference through coordination of the heteroatom to palladium. Thus, 2-bromopyridine could only be arylated satisfactory at 0.2 mol% catalyst loading (Table 3, entries 5 and 6), while thiophenes seem to poison the catalyst more or less completely (entry 7). Finally, *p*-nitrobenzyl bromide [13] could also be arylated in the presence of **9** with quite reasonable results (entry 8), again carrying out the reaction open to air.

4. Conclusion

In conclusion, the readily available bis(oxazole) **5b** appears to be an attractive alternative to commonly employed NCN-pincer ligands, as demonstrated for palladium-catalyzed Suzuki-Miyaura coupling reactions, which could be carried out open to air and with low catalyst loading.

Acknowledgments

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