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THE NCN-TYPE PINCER COMPLEX OF PALLADIUM(II) WITH A 2,6-BIS(2-PYRIDYL)-4-*tert*-BUTYLBENZENE TRIDENTATE LIGAND: SYNTHESIS, STRUCTURE AND CATALYTIC ACTIVITY IN THE MIZOROKI-HECK REACTION

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Abstract – The reaction of 1-bromo-4-*tert*-butyl-2,6-diiodobenzene with 2-pyridylzinc chloride in the presence of catalytic Pd(PPh₃)₄ afforded an NCN-type pincer palladium(II) complex with two pyridine donors. The structure of the complex was determined by X-ray crystallography. The complex was found to catalyze the Mizoroki-Heck reaction at 250 °C under aerobic conditions.

INTRODUCTION

Pincer complexes¹ of transition metals are well-known to function as catalysts in a variety of useful organic transformation reactions such as the Mizoroki-Heck reaction,² allylation of aldehydes,³ and dehydrogenation of alkanes.⁴ Pincer ligands are generally composed of an anionic benzene ring with two substituents at the 2,6-positions which bear donor (P, N, S, Se, etc.) groups, and phosphorus donors (PCP-type) are widely applied to the above-described catalytic reactions.

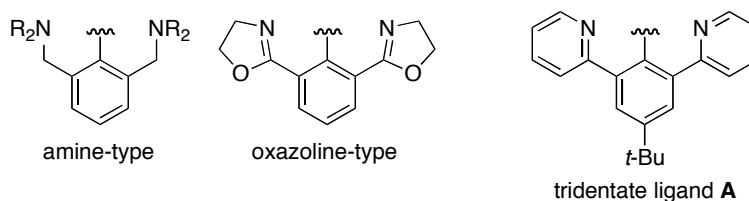
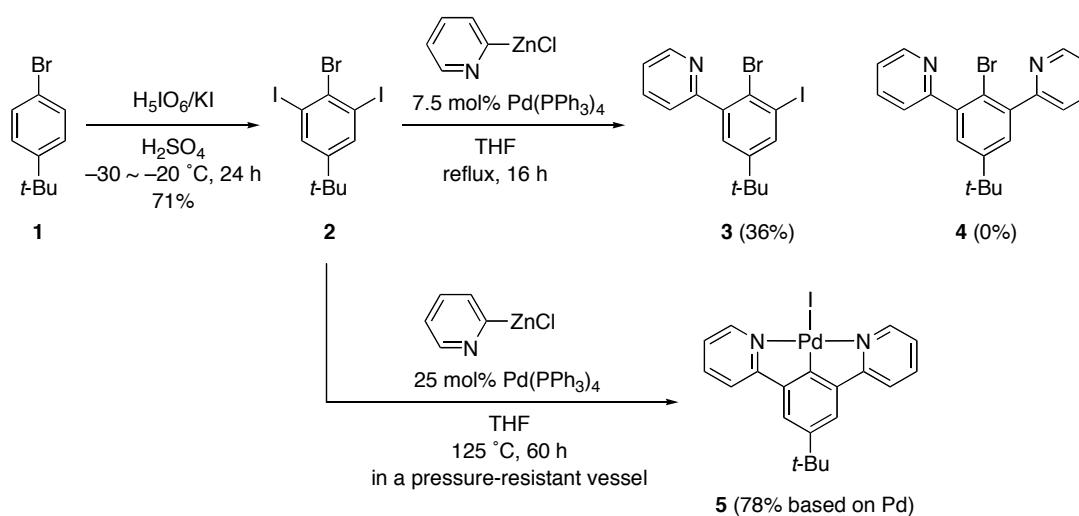


Figure 1

As for pincer ligands with two nitrogen donors (NCN-type), amine- and oxazoline-types are well-known (Figure 1).⁵ However, for the pyridine-type, only a few examples have been reported.⁶⁻⁹ During the course of our study to isolate hypervalent compounds of main group elements such as carbon^{10,11} and boron,^{11,12} we designed a novel tridentate ligand with a 2,6-bis(2-pyridyl)-4-*tert*-butylbenzene skeleton (Figure 1, A). In our several attempts to prepare a ligand precursor, 2,6-bis(2-pyridyl)-1-bromo-4-*tert*-butylbenzene, using a Pd(II)-catalyzed cross-coupling reaction, we accidentally found that an NCN-type Pd(II) pincer complex with two pyridine donors was formed. In this article, the synthesis, structure, and catalytic activity of the NCN-type Pd(II) complex will be described.

RESULTS AND DISCUSSION

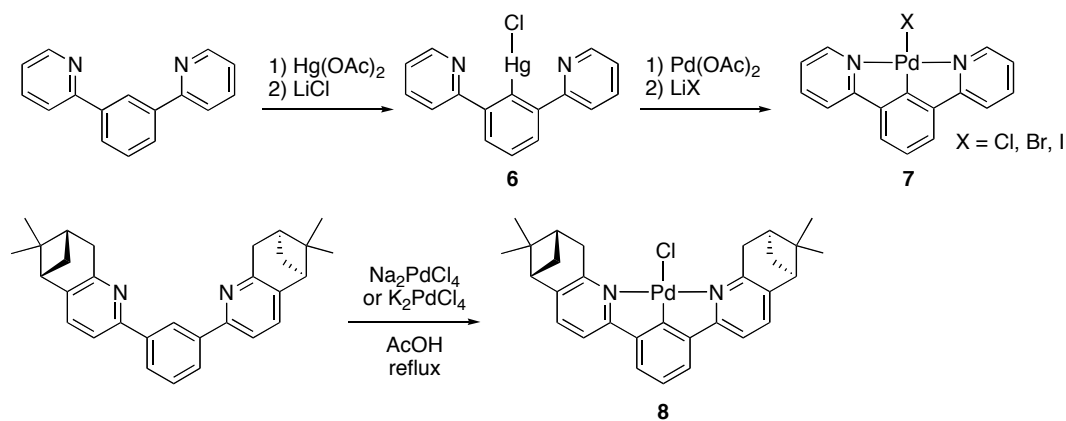
At first, 1-bromo-4-*tert*-butyl-2,6-diiodobenzene (**2**) was prepared from 4-*tert*-butyl-1-bromobenzene (**1**) in 71% yield using the literature method (Scheme 1).¹³ The cross-coupling of **2** with 2-pyridylzinc chloride was then performed in refluxing THF to give a monopyridylated compound (**3**) in low yield (36%), but the desired compound (**4**) was not observed at all. Thus, when the reaction was performed at 125 °C in a pressure-resistant vessel using 25 mol% of catalyst, the formation of an NCN pincer palladium complex (**5**) was observed. This clearly indicates that compound **4** which is formed by the coupling reaction immediately reacts with the catalyst Pd(PPh₃)₄, followed by an exchange of the halogen atom attached to Pd (Br to I) to afford **5**. Complex **5** was isolated by silica-gel column chromatography, and the isolated yield was 78% based upon the amount of Pd(PPh₃)₄ used.



Scheme 1

The reported methods for the synthesis of NCN pincer Pd(II) complexes with pyridine donors involved stepwise reactions, i.e., the 1,3-bis(2-pyridyl)benzene derivative was prepared, then the palladium atom was introduced.⁷⁻⁹ At the step for introducing the palladium atom, Soro et al. used

2,6-bis(2-pyridyl)phenylmercury chloride (**6**) as the synthetic intermediate to prepare complex **7** (Scheme 2).⁷ Later, Soro et al.⁸ and Ahn et al.⁹ independently developed the direct insertion of palladium by C-H activation using a tetrachloropalladate salt to afford **8**. However, our method can incorporate both the two donor ligands and the palladium atom in a one-pot reaction.



Scheme 2

Single crystals of **5** were grown by slow evaporation of a dichloromethane solution at room temperature. The crystal structure of **5** was determined by X-ray crystallography (Figure 2). The three aromatic rings, and the palladium and iodine atoms are on the same plane, and the palladium atom takes on a distorted square planar geometry with an N1—Pd—N2 angle of 159.5(3)°. The overall structure is quite similar to that of Soro's compound **7** (X = Cl).⁷

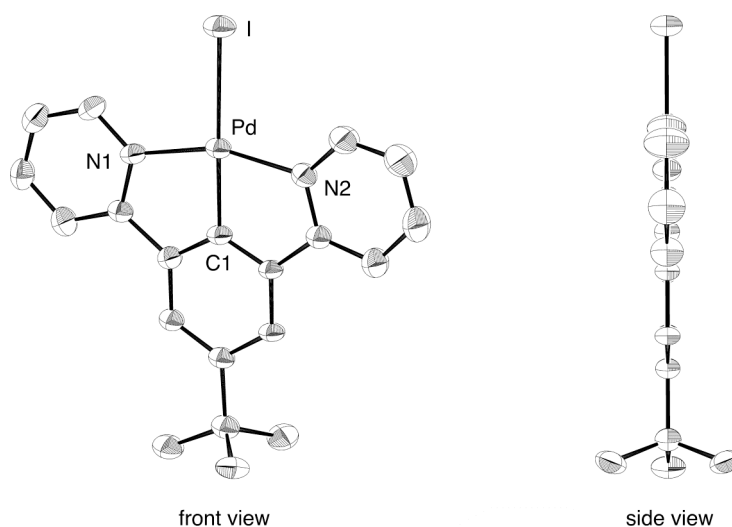


Figure 2. The ORTEP drawing of palladium complex **5** with the thermal ellipsoids shown at the 30% probability level. The hydrogen atoms and the solvent (dichloromethane) were omitted for clarity. Selected bond lengths (Å) and angles (°) for **5**: Pd—I, 2.7351(8); Pd—N1, 2.073(7); Pd—N2, 2.073(7); Pd—C1, 1.944(7); I—Pd—N1, 101.83(17); I—Pd—N2, 98.68(19); I—Pd—C1, 178.6(2); N1—Pd—N2, 159.5(3); N1—Pd—C1, 79.6(3); N2—Pd—C1, 79.9(3).

Because complex **5** was stable even at 300 °C under air, we examined the catalytic activity of **5** in the Mizoroki-Heck reaction¹⁴ under aerobic conditions. The results are summarized in Table 1. At the reaction temperature of 120 °C (entries 1 and 3), catalytic activities were little observed. However, when a higher reaction temperature (250 °C) was employed (entries 2, 4 and 5), the reactions proceeded to afford the corresponding olefins with high *trans* selectivities. It should be noted that complex **5** still remains after these reactions. The turnover numbers of **5** (~2,000) are two orders of magnitude lower than the Soro's results (~100,000).⁷ This may be due to the choice of the base (NEt₃ or Na₂CO₃) and the gradual decomposition of complex **5** under our aerobic conditions.

Table 1. The catalytic activity of **5** in the Mizoroki-Heck reaction under air^a

$$\text{ArX} + \text{CH}_2=\text{CH-R} \xrightarrow[\text{DMF}]{\text{5, Na}_2\text{CO}_3} \text{Ar-CH=CH-R}$$

entry	ArX	R	5 (mol%)	temp (°C)	time (h)	product	TON ^b
1	PhI	Ph	1.0	120	5	<i>trans</i> (1.3%)	1.3
2	PhI	Ph	0.04	250	25	<i>trans</i> (82%), <i>cis</i> (trace)	2140
3	PhBr	Ph	1.0	120	5	—	—
4	PhBr	Ph	0.04	250	25	<i>trans</i> (50%), <i>cis</i> (trace)	1300
5	PhI	CO ₂ Bu	0.04	250	25	<i>trans</i> (74%)	1930

[a] Reaction conditions: ArX (5 mmol), olefin (6 mmol), Na₂CO₃ (6 mmol), DMF (3

mL). [b] TON = turnover number (= mol of product/mol of catalyst).

In summary, we demonstrated the novel synthesis of the NCN pincer palladium(II) complex (**5**) using the one-pot introduction of two pyridine donors and a palladium atom into 1-bromo-4-*tert*-butyl-2,6-diiodobenzene (**2**). The solid state structure of **5** was unambiguously determined by the single-crystal X-ray crystallography. In the Mizoroki-Heck reaction, complex **5** showed the catalytic activity even under aerobic conditions, showing the high robustness of **5** to air. Further investigations on the application of **5** as catalyst, involving oxidation of alkanes with molecular oxygen, are now in progress.

EXPERIMENTAL

General

The melting points were measured using a Yanaco micro melting point apparatus. The ¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra were recorded using a JEOL EX-400 or a JEOL AL-400 spectrometer. The ¹H NMR chemical shifts (δ) are given in ppm downfield from Me₄Si, determined by residual CHCl₃ (δ 7.26). The ¹³C NMR chemical shifts (δ) are given in ppm downfield from Me₄Si,

determined by CDCl_3 (δ 77.0). Elemental analyses were performed using a Perkin-Elmer 2400 CHN elemental analyzer. Tetrahydrofuran (THF) was freshly distilled from Na-benzophenone. Merck silica gel 60 was used for the column chromatography.

1-Bromo-4-*tert*-butyl-2,6-diiodobenzene (2)

To a 1000 mL flask equipped with a mechanical stirrer were added conc. H_2SO_4 (500 mL) and periodic acid (22.8 g, 100 mmol). After the dissolution of periodic acid, KI (49.8 g, 300 mmol) was added in small portions to produce a deep purple solution. To the solution was added dropwise 4-bromo-1-*tert*-butylbenzene (42.6 g, 200 mmol) at -30°C . The mixture was stirred for 24 h while maintaining the temperature between -30 and -20°C . The mixture was then poured onto ice and filtered. The residue was taken up in CH_2Cl_2 , washed with 5% NaOH aq. (200 mL x 3) and H_2O (200 mL x 2), and dried over anhydrous MgSO_4 . After filtration, ethanol (100 mL) was added to the filtrate, CH_2Cl_2 was evaporated and the resulting white precipitate was collected by filtration. The filtrate was concentrated to give another crop of crystals. The combined solids were purified by column chromatography on silica gel using hexane as eluent to give 1-bromo-4-*tert*-butyl-2,6-diiodobenzene (66.0 g, 142 mmol, 71%) as a white solid. ^1H NMR (CDCl_3) δ 7.82 (s, 2H), 1.27 (s, 9H). ^{13}C NMR (CDCl_3) δ 153.6 (C), 137.1 (CH), 132.6 (C), 99.8 (C), 34.3 (C), 30.9 (CH_3). mp $67-69^\circ\text{C}$. Anal. Calcd for $\text{C}_{10}\text{H}_{11}\text{BrI}_2$ (464.91): C 25.83, H 2.38. Found: C 25.94, H 2.33.

Attempted synthesis of 4 in refluxing THF ~ Isolation of 3 ~

Under Ar, to a solution of 2-bromopyridine (0.97 mL, 10 mmol) in THF (20 mL) under Ar at -78°C was added dropwise *n*-BuLi in *n*-hexane solution (7.6 mL, 1.57 M, 12 mmol) with vigorous stirring, and the stirring was continued for 1.5 h at -78°C . A 1 M ZnCl_2 solution in ether (12 mL, 12 mmol) was added dropwise, and the mixture was stirred for 10 min at the same temperature, then allowed to warm up to room temperature and stirred for 1.5 h. The resulting solution was then concentrated to ca. 10 mL in vacuo. The solution was added to a mixture of 1-bromo-4-*tert*-butyl-2,6-diiodobenzene (1.39 g, 4.00 mmol) and $\text{Pd}(\text{PPh}_3)_4$ (350 mg, 0.300 mmol) under Ar atmosphere. The mixture was concentrated to ca. 5 mL, then refluxed for 16 h. The resulting mixture was allowed to cool to rt, then diluted with CH_2Cl_2 and filtered. The filtrate was evaporated to dryness. The residue was purified by column chromatography on silica gel using CH_2Cl_2 as eluent to afford 1-bromo-2-iodo-6-(2-pyridyl)-4-*tert*-butylbenzene (**3**) (453 mg, 1.09 mmol, 36%), but the desired **4** was not detected. **3**: ^1H NMR (CDCl_3) δ 1.31 (s, 9H), 7.32 (t, $J = 5$ Hz, 1H), 7.40 (d, $J = 2$ Hz, 1H), 7.50 (d, $J = 8$ Hz, 1H), 7.78 (t, $J = 8$ Hz, 1H), 7.92 (d, $J = 2$ Hz, 1H), 8.70 (d, $J = 5$ Hz, 1H).

Attempted synthesis of **4 at 125 °C ~ Isolation of palladium complex **5** ~**

Under Ar, to a solution of 2-bromopyridine (1.9 mL, 20 mmol) in THF (100 mL) at –78 °C was added dropwise *n*-BuLi in *n*-hexane solution (14 mL, 1.60 M, 22 mmol) with vigorous stirring, and the stirring was continued for 1 h at –78 °C. A 1 M ZnCl₂ solution in ether (22 mL, 22 mmol) was added dropwise, and the mixture was stirred for 10 min at the same temperature, then allowed to warm up to rt and stirred for 3.5 h. The resulting solution was then concentrated to ca. 30 mL in vacuo. The solution was added to a mixture of 1-bromo-4-*tert*-butyl-2,6-diiodobenzene (1.86 g, 4.00 mmol) and Pd(PPh₃)₄ (1.16 g, 1.00 mmol) in a pressure-resistant vessel. The mixture was heated for 60 h at 125 °C. The resulting mixture was allowed to cool to rt, then poured into saturated aqueous EDTA disodium salt. To the mixture was added aqueous NaHCO₃ until the pH = ca. 8. The mixture was extracted with CH₂Cl₂ (250 mL) and washed with H₂O (50 mL x 2). The organic layer was dried over Na₂SO₄ and evaporated to dryness. The crude product was purified by column chromatography (CH₂Cl₂) to give 2,6-bis(2-pyridyl)-4-*tert*-butylphenylpalladium(II) iodide (**5**) (406 mg, 0.780 mmol, 78% based on Pd) as yellow needles. Single crystals of **5** suitable for X-ray crystallography were obtained by slow evaporation of a CH₂Cl₂ solution. **5**: ¹H NMR (CDCl₃) δ 9.49 (d, *J* = 6 Hz, 2H), 7.79 (t, *J* = 8 Hz, 2H), 7.63 (d, *J* = 8 Hz, 2H), 7.37 (s, 2H), 7.14 (dd, *J* = 8 Hz, *J* = 6 Hz, 2H), 1.34 (s, 9H). ¹³C NMR (CDCl₃) δ 168.9 (C), 164.7 (C), 156.9 (CH), 148.0 (C), 143.0 (C), 138.5 (CH), 123.5 (CH), 121.1 (CH), 118.9 (CH), 35.1 (C), 31.6 (CH₃). mp >300 °C. Anal. Calcd for C₂₀H₁₉IN₂Pd (520.70): C 46.13, H 3.68, N 5.38. Found C 46.62, H 3.85, N 5.18.

General procedure for the Mizoroki-Heck reaction

DMF (3 mL) was added to a mixture of aryl halide (5.00 mmol), olefin (6.00 mmol), **5** (50.0 or 1.92 μmol), and Na₂CO₃ (645 mg, 6.00 mmol) in a pressure-resistant vessel. The mixture was heated for 5 h (or 25 h) at 120 °C (or 250 °C). The mixture was allowed to cool to rt, then extracted with Et₂O (100 mL) and washed with H₂O (100 mL x 2). The organic layer was dried over Na₂SO₄ and evaporated to dryness. The residue was subjected to column chromatography to give the corresponding olefinic product.

Single crystal X-ray analysis of **5.**

A single crystal suitable for the X-ray structural determination was mounted on a Mac Science DIP2030 imaging plate diffractometer and irradiated with graphite monochromated Mo-*K*α radiation (λ = 0.71073 Å) at 293 K for data collection. The unit cell parameters were determined by separately autoindexing several images in each data set using the DENZO program (MAC Science).¹⁵ For each data set, the rotation images were collected in 3 degree increments with a total rotation of 180 deg about the φ axis. The data were processed using SCALEPACK. The structure was solved by a direct method with the SHELXS-97 program.¹⁶ Refinement on *F*² was carried out using the full-matrix least-squares by the

SHELXL-97 program.¹⁶ All non-hydrogen atoms were refined using the anisotropic thermal parameters. The hydrogen atoms were included in the refinement along with the isotropic thermal parameters. Crystallographic data for **5**: orthorhombic system, space group *Pnma* (no. 62), $a = 13.8010(6)$ Å, $b = 6.87300(10)$ Å, $c = 23.6280(9)$ Å, $V = 2241.22(13)$ Å³, $Z = 4$, $D_{\text{calc}} = 1.795$ g cm⁻³, data/param = 2619/162, R_1 ($I > 2\sigma(I)$) = 0.0637, wR_2 (all data) = 0.2017, $GOF = 1.233$.

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