

Synthesis and structural characterization of the first unsymmetrical diarylpalladium complex *trans*-Pd(C₆F₅)(2,4,6-C₆F₃H₂)(PEt₃)₂, derived from transmetallation between 2,4,6-trifluorophenylboronic acid and *trans*-Pd(C₆F₅)I(PEt₃)₂

Yasushi Nishihara, Hiroyuki Onodera and Kohtaro Osakada*

Chemical Resources Laboratory, Tokyo Institute of Technology, Nagatsuta, Midori-ku, Yokohama 226-8503, Japan. E-mail: kosakada@res.titech.ac.jp; Fax: +81 45 924 5224; Tel: +81 45 924 5224

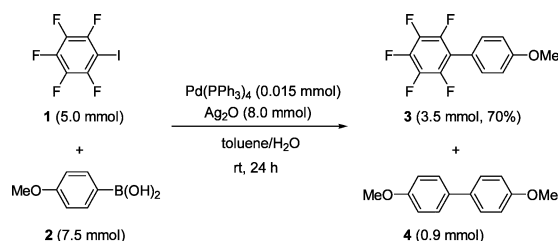
Received (in Cambridge, UK) 30th July 2003, Accepted 5th November 2003

First published as an Advance Article on the web 4th December 2003

The reactions of 2,4,6-trifluorophenylboronic acid with aryl(iodo)palladium(II) complexes, *trans*-Pd(C₆F₅)I(PR₃)₂ (PR₃ = PEt₃, PMe₂Ph, PMePh₂) in the presence of Ag₂O afforded *trans*-Pd(C₆F₅)(2,4,6-C₆F₃H₂)(PR₃)₂ which are stabilized by fluorine atoms in the *ortho* positions.

Palladium catalyzed cross-coupling reactions of aryl halides and arylboronic acids (Suzuki–Miyaura reaction)^{1,2} constitute an exciting development in synthetic organic chemistry. Still the mechanistic features of this reaction are not as clear as those of cross-coupling reactions employing organomagnesium³ and organotin compounds.⁴ The proposed catalytic cycle⁵ involves: (a) oxidative addition of aryl halides to the Pd(0) catalyst; (b) transmetallation of an aryl group from boron to palladium forming intermediate *trans*-diarylpalladium(II) complexes; (c) isomerization of the *trans* to the *cis*; and (d) reductive elimination of unsymmetrical biaryl products thereby regenerating the catalyst. Among these individual reactions, transmetallation is of a special interest. This process likely plays a key role in a large number of important cross-coupling reactions including cleavage of carbon–metal bonds and formation of new C–C bonds. Due to facile reductive elimination, no reports describing the isolation and full characterization of intermediate diarylpalladium complexes via the transmetallation of arylboronic acids with arylpalladium halides have appeared.⁶ On the other hand, Canary et al. have reported the observation by electrospray ionization mass spectroscopy (ESI-MS) of diarylpalladium complexes derived from a mixture of arylboronic acids and aryl(halogeno)palladium(II) complexes. However, the observed spectra are contaminated with the starting Pd complex.⁷ Independently, we isolated diarylplatinum complexes in the transmetallation of organosilicon compounds thereby realizing that Ag₂O can accelerate the transmetallation.⁸ In this paper we report preliminary results on the reactions of various arylboronic acids with aryl(iodo)palladium(II) complexes in the presence of Ag₂O⁹ including the first characterization of an unsymmetrical diarylpalladium(II) complex by X-ray diffraction.

We first examined the catalytic reaction of pentafluoroiodobenzene (1) with 4-methoxyphenylboronic acid (2) in the presence of 3 mol% of Pd(PPh₃)₄ in toluene–H₂O and found the corresponding cross-coupled product 3 in 70% NMR yield, along with some homo-coupled product 4 derived from the added arylboronic acids (Scheme 1). We hypothesized that the generation of cross-coupled products occurred via smooth reductive elimination similar to the catalytic reaction. Reaction in THF–H₂O co-solvent system gave the almost same result.



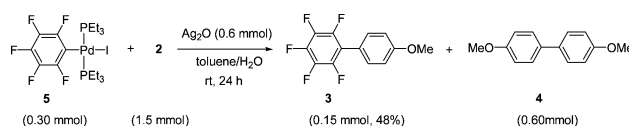
Scheme 1

To isolate the intermediate the rate of reductive elimination was decreased by employing a more basic PEt₃-ligated palladium complex. Thus, when a mixture of *trans*-Pd(C₆F₅)I(PEt₃)₂ (5) and arylboronic acid 2 in the presence of Ag₂O was stirred in toluene–H₂O for 24 h at room temperature, the identical products shown in Scheme 1 were formed, albeit with a lower yield of the cross-coupled product 3 and a higher yield of the homo-coupled product 4 (Scheme 2). We observed the formation of an unidentified palladium complex, indicating that reductive elimination of the cross-coupling product 3 was certainly suppressed, probably due to a strong basicity of PEt₃ ligands. However, our attempt to isolate and characterize the unsymmetrical diarylpalladium complex was unsuccessful as long as we used 4-methoxyphenylboronic acid as the substrate.

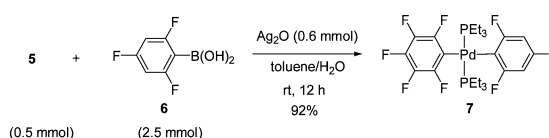
On the other hand, this observation led us to investigate the reaction of 2,4,6-trifluorophenylboronic acid (6) with 5. The fluorine atoms in the *ortho* positions are expected to retard reductive elimination of the initially formed diarylpalladium complex. With this strategy a new unsymmetrical diarylpalladium complex, *trans*-Pd(C₆F₅)(2,4,6-C₆F₃H₂)(PEt₃)₂ (7), was isolated in 92% yield (Scheme 3).†

The structure of 7 was determined by X-ray analysis of a single crystal grown from slow evaporation of hexane solution.‡ As seen in Fig. 1, the molecular structure of 7 shows a palladium atom in an approximately square-planar environment. The aryl planes lie perpendicular to the coordination plane, similar to the square-planar *trans*-diarylpalladium(II) complex.¹⁰

To the best of our knowledge, no report of the synthesis of a stable unsymmetrical diarylpalladium(II) complex by transmetallation in the reactions of arylboronic acids and transition metal complexes has appeared.¹¹ In the solid state, 7 can be stored in air for months, without any sign of decomposition. Even upon heating at 100 °C for 24 h in toluene-*d*₆, complex 7 does not produce a cross-coupled product. Since no signal assigned to a *cis* isomer was observed during heating, the fluorine substituents in the *ortho* position retard *trans*–*cis* isomerization leading towards reductive elimination. The ¹H, ¹⁹F{¹H}, and ³¹P{¹H} NMR spectra of 7 in rigorously dry solvents, e.g., C₆D₆, CDCl₃, and CD₂Cl₂, indicate that all ligands on the Pd atom are inert and that reductive elimination of biaryl does not occur. The ³¹P{¹H} NMR spectrum of 7 in C₆D₆ consists of a singlet at δ 15.88, which is typical of Pd(II) complexes possessing two *trans* phosphine ligands. The *ipso*



Scheme 2



Scheme 3

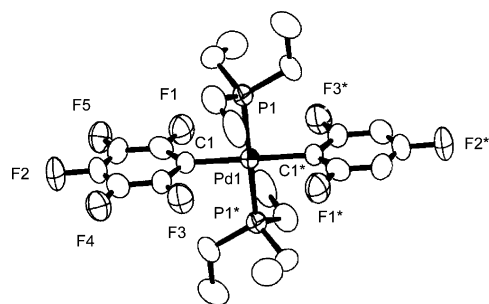


Fig. 1 An ORTEP drawing of **7** with 50% thermal ellipsoidal plotting. The molecule has crystallographic C_2 symmetry within the molecule. Atoms with asterisks are crystallographically equivalent to those having the same numbers without asterisks. Fluorine (F4* and F5*) with occupancies of 0.5 and hydrogen atoms were omitted for clarity. Selected interatomic distances (Å) and angles (°): Pd1–C1 2.066(6), Pd1–P1 2.310(2), P1–Pd1–C1 88.5(2), P1–Pd1–C1* = 91.5(2).

carbon signals of the aryl ligands are observed as triplets at δ 121.30 and 126.67. These NMR data are similar to those of the previously reported *trans*-PdAr₂(PEt₃)₂¹² and are consistent with the trans structure in solution.

We evaluated the transmetalation rate by the reactions of 2,4,6-trifluorophenylboronic acid with *trans*-Pd(C₆F₅)I(PR₃)₂ (PR₃ = PEt₃, PMe₂Ph, PMePh₂) forming *trans*-Pd(C₆F₅)(2,4,6-C₆F₃H₂)(PR₃)₂ (**7**: PR₃ = PEt₃; **8**: PR₃ = PMe₂Ph; **9**: PR₃ = PMePh₂). The observed rates of formation of diarylpalladium(II) complexes increase in the following order, **7** (12 h) < **8** (3 h) < **9** (40 min) at room temperature. This result correlates with the order of pK_a of the phosphine ligand, e.g. PEt₃ (8.65) < PMe₂Ph (6.50) < PMePh₂ (4.65).¹³

The reaction of Ag₂O with **5** (1.2 : 1.0 molar ratio) in toluene–H₂O generated *trans*-Pd(C₆F₅)(OH)(PEt₃)₂ (**10**) with concomitant generation of AgI. The ³¹P{¹H} NMR measurement of the above reaction mixture in C₆D₆ showed that a signal of the starting material **5** at δ 16.41 decreased with appearance of a new signal at δ 18.50, which is identical with that of **10**, synthesized independently.¹⁴ The ¹H NMR spectrum of **10** exhibits a resonance at δ –2.40, diagnostic of the Pd–OH, while the ¹³C{¹H} NMR signal of the PCH₂ carbon appears at δ 14.19 as an apparent triplet due to virtual coupling, indicating *trans* positions of two phosphorus atoms. These results suggest an explanation for the role of Ag₂O, which promotes to replace the iodo ligand of **5** with a OH group of H₂O to afford **10**, the intermediate of transmetalation. Further details of the mechanism of transmetalation are still unclear.

In summary, we have successfully isolated diarylpalladium complexes **7–9** from the reactions of arylboronic acids with aryl(iodo)palladium(II) complexes. This methodology provides a novel and potentially practical synthetic method for unsymmetrical diaryl complexes of Pd, which are normally synthesized using organolithium and organomagnesium compounds.¹⁵ Extensive exploration of this approach using the analogous arylboronates to illuminate more mechanistic details of the Suzuki–Miyaura cross-coupling reaction will be reported in due course.

Notes and references

† *Selected data.* For **7**: colorless crystals, yield 92%. δ_H (300 MHz, C₆D₆): 0.80 (dt, J = 16 Hz, 8 Hz, 18H, CH₃), 1.02 (m, 12H, PCH₂), 6.51 (dd, J = 9 Hz, 5 Hz, 2H, C₆H₂), δ_F (121.5 MHz, C₆D₆, 85% H₃PO₄): 15.88 (s), δ_F (282.3 MHz, C₆D₆): –82.45 (s, 2F), –112.14 (d, J = 24 Hz, 2F), –115.92 (m, 1F), –158.60 (t, J = 20 Hz, 1F), –160.51 (m, 2F). Anal. Calc. for C₂₄H₃₂F₈P₂Pd: C, 44.98; H, 5.03; F, 23.72. Found: C, 44.90; H, 4.94; F, 24.06%. For **8**: colorless crystals, yield 77%. δ_H (300 MHz, C₆D₆): 0.98 (apparent triplet by virtual coupling, 12H, PCH₃), 6.39 (dd, J = 9 Hz, J =

5 Hz, 2H, C₆H₂F₃), 6.87–6.95 (m, 6H, Ph), 7.00–7.07 (m, 4H, Ph). δ_F (121.5 MHz, C₆D₆, 85% H₃PO₄): –4.54 (s), δ_F (282.3 MHz, C₆D₆): –84.91 (t, J = 5 Hz, 2F), –114.41 (d, J = 24 Hz, 2F), –115.99 (t, J = 7 Hz, 1F), –159.51 (t, J = 21 Hz, 1F), –161.00 (m, 2F). Anal. Calc. for C₂₈H₂₄F₈P₂Pd: C, 49.40; H, 3.55; F, 22.32. Found: C, 49.14; H, 3.75; F, 22.33%. For **9**: colorless crystals, yield 47%. δ_H (300 MHz, C₆D₆): 1.46 (apparent triplet by virtual coupling, 6H, CH₃), 6.15 (dd, J = 9 Hz, J = 5 Hz, 2H, C₆H₂F₃), 6.88–6.93 (m, 12H, Ph), 7.30–7.37 (m, 8H, Ph). δ_F (121.5 MHz, C₆D₆, 85% H₃PO₄): 9.77 (s), δ_F (282.3 MHz, C₆D₆): –83.29 (t, J = 5 Hz, 2F), –113.23 (d, J = 23 Hz, 2F), –116.50 (t, J = 9 Hz, 1F), –160.28 (t, J = 20 Hz, 1F), –160.95 (m, 2F). Anal. Calc. for C₃₈H₂₈F₈P₂Pd: C, 56.70; H, 3.51; F, 18.88. Found: C, 56.50; H, 3.71; F, 19.24%.

‡ *Crystal data.* For **7**: C₂₄H₃₂F₈P₂Pd, M = 640.85, monoclinic, space group $P2_1/n$, a = 12.309(4), b = 12.207(5), c = 9.460(3) Å, β = 104.81(3)°, V = 1374.2(8) Å³, Z = 2, T = 298 K, μ (Mo–K α) = 8.57 cm^{–1}, Rigaku AFC7R diffractometer, 1739 measured reflections ($2\theta_{max}$ = 55.0°). At convergence, $R1$ = 0.032, $wR2$ = 0.037, and GOF = 2.02 for 169 variables refined against all 1077 unique reflections. A space group $C2/m$ is excluded by the presence of reflections ($I > 10\sigma(I)$) that do not obey the reflection conditions of C (or I) lattice. CCDC 216136. See <http://www.rsc.org/suppdata/cc/b3/b308741g/> for crystallographic data in .cif or other electronic format.

- For reviews for cross-coupling reactions of organoboron compounds, see: A. Suzuki, *Pure Appl. Chem.*, 1986, **58**, 629–638; A. Suzuki, *J. Organomet. Chem.*, 1999, **576**, 147–168.
- J. Uenishi, J.-M. Beau, R. W. Armstrong and Y. Kishi, *J. Am. Chem. Soc.*, 1987, **109**, 4756–4758.
- F. Ozawa, K. Kurihara, M. Fujimori, T. Hidaka, T. Toyoshima and A. Yamamoto, *Organometallics*, 1989, **8**, 180–188.
- A. L. Casado, P. Espinet and A. M. Gallego, *J. Am. Chem. Soc.*, 2000, **122**, 11771–11782; A. L. Casado and P. Espinet, *J. Am. Chem. Soc.*, 1998, **120**, 8978–8985.
- N. Miyaura and A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457–2483.
- The vinylrhodium complex was formed by the reaction between the vinylboronic ester and the methoxorhenium complex via a vinyl group transfer. R. D. Simpson and R. G. Bergman, *Organometallics*, 1992, **11**, 3980–3993.
- A. O. Aliprantis and J. W. Canary, *J. Am. Chem. Soc.*, 1994, **116**, 6985–6986.
- N. Mintcheva, Y. Nishihara, M. Tanabe, K. Hirabayashi, A. Mori and K. Osakada, *Organometallics*, 2001, **20**, 1243–1246; N. Mintcheva, Y. Nishihara, A. Mori and K. Osakada, *J. Organomet. Chem.*, 2001, **629**, 61–67.
- Ag₂O promoted Suzuki–Miyaura reactions have been reported; see: F. S. Ruel, M. Braun and C. R. Johnson, *Org. Synth.*, 1997, **74**, 69–77.
- R. Uson, A. Laguna, J. Forniés and I. Valenzuela, *J. Organomet. Chem.*, 1984, **273**, 129–139; P. G. Jones, *J. Organomet. Chem.*, 1988, **345**, 405–411.
- F. Ozawa, T. Hidaka, T. Yamamoto and A. Yamamoto, *J. Organomet. Chem.*, 1987, **330**, 253–263.
- G. Lopez, G. Garcia, M. D. Santana, G. Sanchez, J. Ruiz, J. A. Hermoso, A. Vegas and M. Martinez-Ripoll, *J. Chem. Soc., Dalton Trans.*, 1990, 1621–1626; F. Ozawa, M. Fujimori, T. Yamamoto and A. Yamamoto, *Organometallics*, 1986, **5**, 2144–2149; R. Uson, J. Forniés, F. Martínez, M. Tomas and I. Reoyo, *Organometallics*, 1983, **2**, 1386–1390; R. Uson, J. Forniés, P. Espinet, F. Martínez and M. Tomas, *J. Chem. Soc., Dalton Trans.*, 1981, 463–465; R. Ceder, J. Granell, G. Muller, O. Rossell and J. Sales, *J. Organomet. Chem.*, 1979, **174**, 115–120; R. Uson, J. Forniés, R. Navarro, M. P. Garcia and B. Bergareche, *Inorg. Chim. Acta*, 1977, **25**, 269–271; R. Uson, J. Forniés and F. Martínez, *J. Organomet. Chem.*, 1977, **132**, 429–437; G. W. Parshall, *J. Am. Chem. Soc.*, 1974, **96**, 2360–2366.
- G. M. Kosolapoff and L. Maier, *Organic phosphorus compounds*, Wiley-Interscience, New York, **Vol. 1**, 1972.
- Complex **10** was obtained according to the preparation procedure of *trans*-Pd(C₆F₅)(OH)(PPh₃)₂ and *trans*-PdPh(OH)(PR₃)₂ (R = Cy, ⁱPr); see: T. Yoshida, T. Okano and S. Otsuka, *J. Chem. Soc., Dalton Trans.*, 1976, 993–999; V. V. Grushin and H. Alper, *Organometallics*, 1996, **15**, 5242–5245.
- E.-I. Negishi, T. Takahashi and K. Akiyoshi, *J. Organomet. Chem.*, 1987, **334**, 181–194.