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On the Catalytic Cycle of the Palladium-Catalyzed Cross-Coupling Reaction of Alkynylstannane with Aryl Iodide

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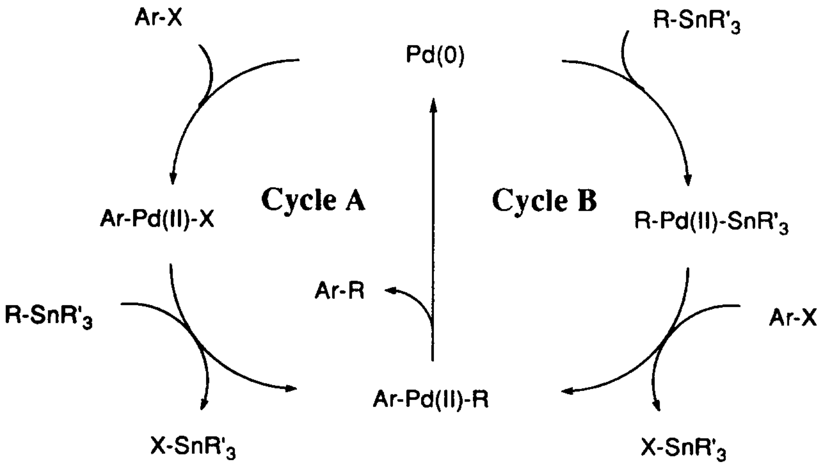
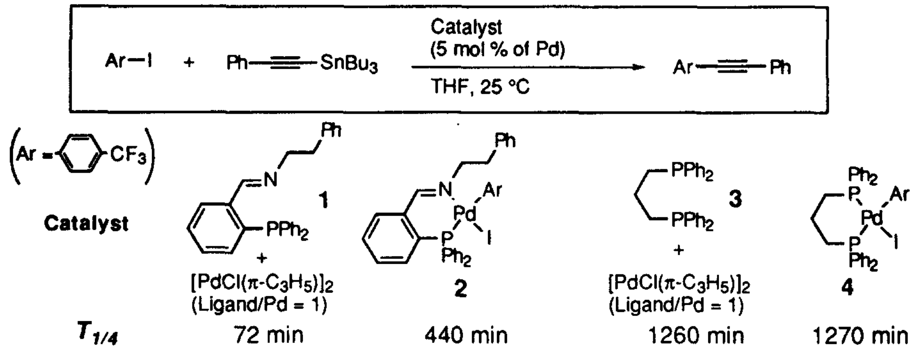
Abstract: The coupling reaction of phenylethynyltributyltin with (4-trifluoromethyl)iodobenzene catalyzed by a Pd(0) complex coordinated by *N*-(2-diphenylphosphinobenzylidene)-2-phenylethylamine was found to start with oxidative addition of the tin reagent to the Pd(0) complex. In contrast, the use of 1,3-bis(diphenylphosphino)propane as the ligand switched the catalytic cycle to the well-accepted one initiated by oxidative addition of the aryl iodide to the Pd(0) complex. © 1997 Elsevier Science Ltd.

A wide variety of organometallics undergo the coupling reaction with aryl halides with the aid of palladium catalysts. Among all, the coupling of organostannanes is widely used particularly in laboratories.[1,2] However, little is known about its reaction mechanism. For example, it still remains uncertain which of the substrate, the electrophile or the organometallic reagent, reacts with a palladium(0) complex. The currently accepted catalytic cycle involves three distinct steps: (1) oxidative addition of aryl halide to an electron-rich palladium(0) complex, (2) transmetalation of the resulting electrophilic palladium(II) complex with a nucleophilic organostannane, and (3) reductive elimination to give a cross-coupled product and regenerate the palladium(0) complex (Scheme 1, Cycle A).[3] We report that Cycle B (Scheme 1) which is initiated by oxidative addition of organostannanes to a palladium(0) complex[4] takes place with alkynylstannane and a palladium(0) complex coordinated by an iminophosphine ligand.[5]

Scheme 1



Scheme 2



First, we examined the reaction rate of the palladium-catalyzed coupling of phenylethynyltributyltin with (4-trifluoromethyl)iodobenzene (Ar-I), using *N*-(2-diphenylphosphinobenzylidene)-2-phenylethylamine (**1**)[6] or 1,3-bis(diphenylphosphino)propane (**3**) as a ligand (Scheme 2). The complexes **2** and **4**, prepared by the reaction of Ar-I with the corresponding palladium(0) complexes,[7] are the expected intermediates of Cycle A. We assumed that, if the reaction would take place according to Cycle A, no induction period should be observed with these catalysts and that the rates in the early stage of the reaction should be similar to or higher than those with the corresponding catalysts prepared in situ. If this is not the case, another catalytic cycle, Cycle B, must be working. To investigate the rate in the early stage of the reaction, we measured time ($T_{1/4}$) required for 25% conversion. Conversion was monitored on the basis of consumed Ar-I by ^{19}F NMR of the reaction mixture. When complex **2** or **4** was used, the product derived from the complex also was counted in conversion.

We found that $T_{1/4}$ with preformed catalyst **2** was 440 min, much larger than $T_{1/4}$ (= 72 min) obtained with the catalyst prepared in situ from **1** and $[PdCl(\pi\text{-}C_3H_5)]_2$. This means that the catalyst of **1**–$[PdCl(\pi\text{-}C_3H_5)]_2$ did not mediate the coupling reaction according to Cycle A. In contrast, the catalysts prepared with diphosphine **3**, both preformed and prepared in situ, promoted the reaction at almost the same rates, $T_{1/4}$ being 1270 and 1260 min, respectively. These results suggest that in these cases Cycle A is involved.

We next studied by $^{31}P\{^1H\}$ NMR the behavior of the palladium complex during the reaction (Figures 1 and 2). Since oxidative addition of Ar-I to a palladium(0) complex coordinated by **1** or **3** is irreversible,[8] complex **2** or **4**,[9] once produced, cannot but get into Cycle A.

The peaks of complex **4** predominated in the reaction catalyzed by **3**–$[PdCl(\pi\text{-}C_3H_5)]_2$ (Figure 1), showing that the reaction proceeded according to Cycle A and that transmetalation was the rate-determining-

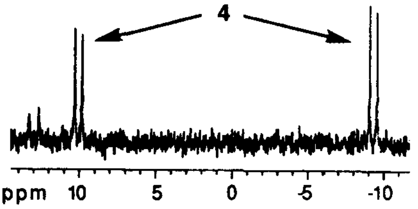


Figure 1. $^{31}P\{^1H\}$ NMR (109 MHz) spectrum of the reaction mixture (at *ca.* 38% conversion) of **3**–$[PdCl(\pi\text{-}C_3H_5)]_2$-catalyzed coupling of phenylethynyltributyltin with Ar-I in THF.

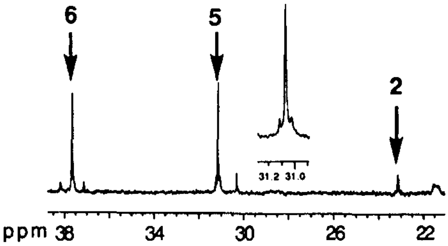
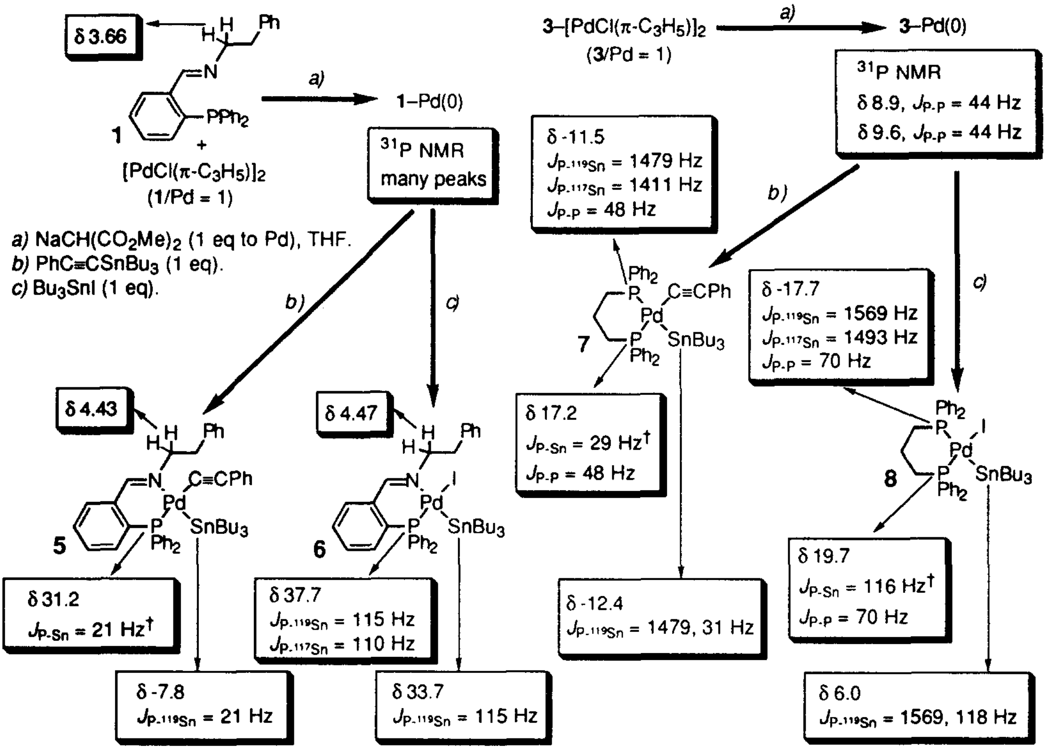


Figure 2. $^{31}P\{^1H\}$ NMR (109 MHz) spectrum of the reaction mixture (at 2-33% conversion) of **1**–$[PdCl(\pi\text{-}C_3H_5)]_2$-catalyzed coupling of phenylethynyltributyltin with Ar-I in THF.

step.[10] By contrast, the reaction with 1–[PdCl(π-C_3H_5)]$_2$ showed only a small amount of complex **2** (Figure 2). If the reaction proceeded along Cycle A, complex **2** must be observed dominantly as above because the rate-determining-step should be transmetalation.[10]

Two major species observed in the reaction catalyzed by 1–[PdCl(π-C_3H_5)]$_2$ were identified as **5** and **6** (Figures 2 and 3[11]). Each of the complexes[12] was characterized as follows: (1) Formation of a Pd–Sn bond was confirmed by a large shift in ^{119}Sn resonance, (2) coordination of the nitrogen atom was validated by the downfield shift (*ca.* 0.8 ppm) of the methylene protons adjacent to the nitrogen atom, and (3) the *cis*-configuration of the phosphino and stannyl groups was assigned on the basis of small coupling constants between phosphorous and tin atoms.[4a,4b,4d] Although the stoichiometric reaction of **3**–Pd(0) with phenylethynyltributyltin or tributyltin iodide also generated the corresponding species **7** and **8** (Figure 3), they were not detected under the conditions of the cross-coupling reaction (Figure 1).



cf. ^{119}Sn{^{1}H} NMR (THF): δ -67.0 for PhC≡CSnBu$_3$; δ 79.6 for Bu$_3$SnI

† $J_{P\text{-}^{119}Sn}$ and $J_{P\text{-}^{117}Sn}$ were not resolved.

Figure 3. ^{31}P{^{1}H}, ^{119}Sn{^{1}H} and ^{1}H NMR (THF-d_8 or THF) parameters (chemical shift, $J_{Sn\text{-}P}$ and $J_{P\text{-}P}$) of Pd(0) complexes, Pd(0)/**1** and Pd(0)/**3**, and their reaction products with PhC≡CSnBu$_3$ or Bu$_3$SnI.

All these observations suggest that the coupling reaction of phenylethynyltributyltin with Ar-I using **1**–[PdCl(π-C_3H_5)]$_2$ as a catalyst should proceed through oxidative addition of a C–Sn bond of the organostannane to the Pd(0) complex. Namely, Cycle B in Scheme 1 accounts for all of the above observations.

In conclusion, although both of palladium(0) complexes **1**–Pd(0) and **3**–Pd(0) react with phenylethynyltributyltin, giving oxidative addition products, **5** and **7**, respectively, each complex behaves in a different manner: **5** is involved in a catalytic cycle, whereas **7** does not participate in the catalysis. Although details, including the generality, remain yet to be studied, the findings discussed herein provide us with a novel clue for the elucidation of the reaction mechanism of the transition metal-catalyzed cross-coupling reactions.

Acknowledgment:

We thank Professor Tamio Hayashi (Kyoto University) for helpful discussions.

References and Notes:

1 Kosugi, M.; Sasazawa, K.; Shimizu, Y.; Migita, T. *Chem. Lett.* **1977**, 301.

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3 For example, see: Farina, V.; Krishnan, B. *J. Am. Chem. Soc.* **1991**, *113*, 9585.

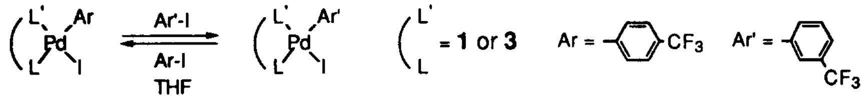
4 There have been many reports concerning oxidative addition of organostannanes to a platinum(0) complexes, which often shows the reactivities similar to palladium(0) complexes. (a) Eaborn, C.; Kundu, K.; Pidcock, A. *J. Chem. Soc., Dalton Trans.* **1981**, 1223. (b) Butler, G.; Eaborn, C.; Pidcock, A. *J. Organomet. Chem.* **1979**, *181*, 47. (c) Butler, G.; Eaborn, C.; Pidcock, A. *J. Organomet. Chem.* **1978**, *144*, C23. (d) Eaborn, C.; Pidcock, A.; Steele, B. R. *J. Chem. Soc., Dalton Trans.* **1976**, 767. (e) Cetinkaya, B.; Lappert, M. F.; McMeeking, J.; Palmer, D. E. *J. Chem. Soc., Dalton Trans.* **1973**, 1202.

5 This type of catalytic cycle was referred without any evidence by Stille and his co-workers in the palladium-catalyzed coupling of acyl chlorides with organostannanes. Labadie, J. W.; Stille, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 6129.

6 We have already reported that the palladium complex coordinated by iminophosphine **1** is an efficient catalyst for the coupling of aryl halides with organostannanes. Shirakawa, E.; Yoshida, H.; Takaya, H. *Tetrahedron Lett.* in press.

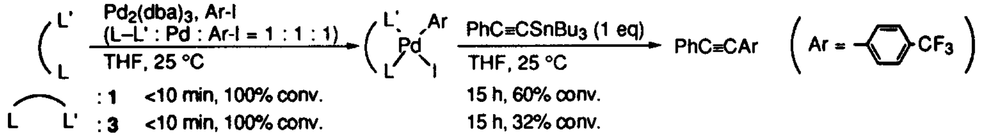
7 For the preparation of **2**, see reference 6. Complex **4** was prepared in a manner similar to **2** and exhibited mp 121-124 °C; ^{1}H NMR (CDCl$_3$) δ 1.6-2.7 (m, 6 H), 6.72-6.77 (m, 2 H), 7.0-7.5 (m, 16 H), 7.70-7.85 (m, 6 H); ^{31}P{^{1}H} NMR (CDCl$_3$) δ -9.7 (J = 54 Hz), 11.0 (J = 54 Hz); ^{19}F NMR (CDCl$_3$, CF$_3$COOH as external standard) δ 13.8. Anal. Calcd for $C_{34}H_{30}P_2F_3IPd$: C, 51.64; H, 3.82. Found: C, 51.48; H, 3.94.

8 Intermolecular exchange of an Ar group shown bellow was not observed at 25 °C in 1 d.



9 ^{31}P{^{1}H} NMR (THF): δ 23.2 for **2**; δ -9.2 (J = 53 Hz), 10.1 (J = 53 Hz) for **4**.

10 Examination under the stoichiometric conditions revealed that transmetalation was the rate-determining-step in Cycle A, as shown by the following data.



11 The procedure for the generation of the Pd(0) complexes depicted in Figure 3 was communicated privately from Professor Tamio Hayashi (Kyoto University).

12 All attempts to isolate these complexes failed because of their instability.

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