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Intramolecular Catalyst Transfer on a Variety of Functional Groups between Benzene Rings in Suzuki-Miyaura Coupling Reaction

Tsutomu Yokozawa*[a], Natsumi Harada, Hajime Sugita, Yoshihiro Ohta

Abstract: Suzuki-Miyaura coupling reaction of BrC_6H_4-X-C_6H_4Br **1** (X = CH_2, CO, N-Bu, O, S, SO, and SO_2) with arylboronic acid **2** was investigated in the presence of ^{t}Bu$_3$PPd precatalyst and CsF/18-crown-6 as a base to establish whether or not the Pd catalyst can undergo catalyst transfer on these functional groups. In the reaction of **1** (X = CH_2, CO, N-Bu, O, and SO_2) with **2**, aryl-disubstituted product **3** (Ar-C_6H_4-X-C_6H_4-Ar) was exclusively obtained, indicating that the Pd catalyst undergoes catalyst transfer on these functional groups. On the other hand, the reaction of **1e** (X = S) and **1f** (X = SO) with **2** afforded only aryl-monosubstituted product **4** (Ar-C_6H_4-X-C_6H_4-Br) and a mixture of **3** and **4**, respectively, indicating that S and SO interfere with intramolecular catalyst transfer. Furthermore, we found that Suzuki-Miyaura polycondensation of **1** (X = CH_2, CO, N-Bu, O, and SO_2) and phenylenediboronic acid **5** in the presence of ^{t}Bu$_3$PPd precatalyst afforded high-molecular-weight polymer even when excess **1** was used. The polymers obtained from **1** (X = CH_2, N-Bu, and O) and **5** turned out to be cyclic.

Many transition metal catalysts have been developed for coupling reactions. For example, Buchwald has improved the efficiency and selectivity of Suzuki-Miyaura coupling reaction by introducing dialkylbiarylphosphine-ligated Pd catalysts.[1] Furthermore, development of the ligands of Pd catalysts has made it possible to conduct C-N[2] and C-O[3] coupling reactions.[4] It has recently been found that Pd and Ni catalysts with certain ligands have a unique propensity for intramolecular catalyst transfer on aromatic rings in polymer chemistry. Thus, Kumada-Tamao,[5] Negishi,[6] and Suzuki-Miyaura[7] coupling polymerizations of AB-type monomer proceed in a living polymerization manner, in which regenerated zero-valent catalyst, after coupling reaction between the propagating end and monomer, moves intramolecularly to the C-X bond of the monomer connected to the propagating end, followed by oxidative addition. We called this type of polymerization catalyst-transfer condensation polymerization (CTCP).[8] Many kinds of well-defined π-conjugated polymers have been synthesized by means of CTCP,[9] as well as many architectures based on π-conjugated polymers.[10] Recently, Stille[11] and Murahashi[12] CTCP have also been reported.

When a Pd catalyst such as ^{t}Bu$_3$PPd, which undergoes intramolecular catalyst transfer, is used for conventional Suzuki-Miyaura polycondensation of dibromoarylene and arylenediboronic acid (ester) (A_2 + B_2 polycondensation), high-molecular-weight π-conjugated polymers with boronic acid (ester) ends are obtained, even if excess dibromo monomer is present under unstochiometric polycondensation conditions.[13] This polymerization behavior is accounted for by successive reaction of dibromoarylene with 2 equivalents of arylenediboronic acid (ester)s through intramolecular catalyst transfer on the π-electron face of dibromoarylene. However, the use of monomers with kinked structures, such as *m*-phenylene, in this type of polycondensation selectively affords cyclic aromatic polymers under unstoichiometric conditions using excess diboromo monomer.[14]

We investigated catalyst transfer on not only aromatic rings, but also multiple bonds between benzene rings in Suzuki-Miyaura coupling reaction. We found that ^{t}Bu$_3$PPd moves on a carbon-carbon double bond (C=C) when alkoxy substituents are attached at the ortho position of the benzene rings connected to C=C,[15] and that intramolecular catalyst transfer takes place on a carbon-carbon triple bond and nitrogen-nitrogen double bond even when there are no substituents on the benzene rings.[16] We had focused on catalyst transfer on π-conjugated systems, and as an extension of that work, we were next interested in whether or not the Pd catalyst can undergo intramolecular catalyst transfer on functional groups located between benzene rings. If this is possible, CTCP could be extended to the synthesis of well-defined engineering plastics containing functional groups such as keto and sulfonyl, as well as ether and sulfide linkages. In this paper, we describe an investigation of intramolecular catalyst transfer on CH_2, CO, N-Bu, O, S, SO, SO_2 by means of Suzuki-Miyaura coupling reaction of dibromo compound **1**, containing these functional groups, with arylboronic acid **2** in the presence of ^{t}Bu$_3$PPd, generated from ^{t}Bu$_3$PPd G2 precatalyst and base. If intramolecular catalyst transfer takes place on the benzene rings and these functional groups in **1** after the first substitution with **2**, disubstituted product **3** should be selectively obtained, rather than monosubstituted product **4** (Scheme 1). We found that the Pd catalyst underwent intramolecular catalyst transfer on CH_2, CO, N-Bu, O, SO_2, and that unstoichiometric polycondensation of excess **1** containing these functional groups with 1 equivalent of *p*-phenylenediboronic acid **5** afforded high-molecular-weight polymers (Scheme 2). Furthermore, the obtained polymers containing the CH_2, N-Bu, O linkages turned out to be cyclic, showing clear peaks in the matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectra.

We first conducted Suzuki-Miyaura coupling reaction of 2 equivalent of **1** containing a variety of functional groups X with 1.0 equivalent of **2** in the presence of 5 mol% of ^{t}Bu$_3$PPd G2 precatalyst and CsF/18-crown-6 as a base at ambient temperature for 3 h (Scheme 1). The product ratio **3**/**4** was determined from the ^{1}H NMR spectra of the crude products (Table 1), and then the products were isolated by column chromatography. When X in **1** was CH_2 (**1a**), only disubstituted product **3** was obtained (Table 1, Entry 1). Similar intramolecular catalyst transfer on disubstituted methylene between thiophenes has been reported in Kumada-Tamao CTCP of bithienylmethane monomer.[17] It seems strange that the Pd catalyst underwent intramolecular transfer on non-conjugated methylene between the benzene rings, but direct transfer from one benzene ring to the other might occur, since the two rings face each other. Incidentally, we have already reported that intramolecular Pd catalyst transfer did not occur on ethylene between benzene rings.[15] Similarly, in the case of oxidized carbon (carbonyl group) in **1**, only disubstituted **3** was obtained (Entry 2). Since 4,4'-dibromobenzophenone **1b** has a planar structure and the carbonyl group is conjugated with two benzene rings, the Pd

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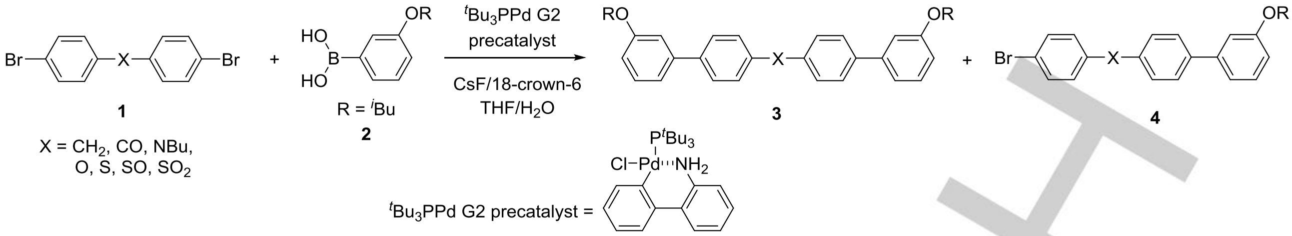
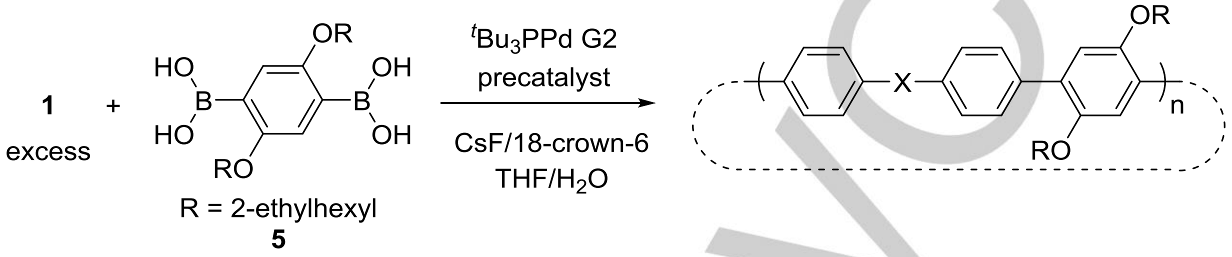
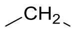
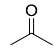
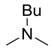
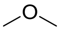
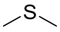
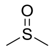
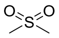


Scheme 1. Suzuki-Miyaura coupling reaction of **1** with **2** in the presence of ^{t}Bu$_3$PPd for investigation of intramolecular catalyst transfer on functional groups X in **1**.



Scheme 2. Unstoichiometric Suzuki-Miyaura polycondensation of excess **1** and 1.0 equivalent of **5** in the presence of ^{t}Bu$_3$PPd.

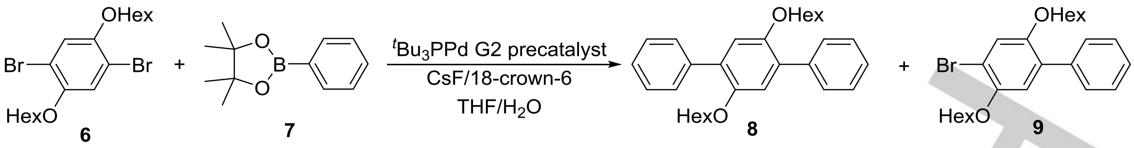
Table 1. Product ratio of **3**/**4** in Suzuki-Miyaura coupling reaction of **1** with **2** in the presence of ^{t}Bu$_3$PPd G2 precatalyst.[a]

Entry	**1**	X in **1**	Conv. of **1**[b]	Yield of **3 + 4**[b,c]	Product ratio **3/4**[b]
1	**1a**		28	25	100/0
2	**1b**		22	22	100/0
3	**1c**		22	23	100/0
4	**1d**		21	21	100/0
5	**1e**		48	48	0/100
6	**1f**		43	37	22/78
7	**1g**		20	22	100/0

[a] Reaction of 2.0 equivalent of **1** and 1.0 equivalent of **2** was carried out with 5 mol% of ^{t}Bu$_3$PPd G2 precatalyst in the presence of CsF (4.0 equivalent) and 18-crown-6 (6.7 equivalent) in THF ([**2**]$_0$ = 50.0 mM) and H$_2$O (THF/H$_2$O = 3.0/0.1 (v/v)) at room temperature for 3 h. [b] Determined from the ^{1}H NMR spectra. [c] Yield is based on **1**.

catalyst should move from one benzene ring to the other through the conjugated π-electron face. Furthermore, the reaction of **1c** (X = N-Bu) and **1d** (X = O) with **2** afforded disubstituted **3** (entries 3 and 4), implying that the lone pairs of N and O did not disturb intramolecular transfer of the Pd catalyst by coordination. In this connection, CTCP of 2-amino-6-bromofluorene by Buchwald-Hartwig amination via intramolecular catalyst transfer on the amino group was recently reported during our work.[18] In contrast to these cases, sulfide **1e** (X = S) gave only monosubstituted **4** (Entry 5),[19] and sulfoxide **1f** (X =SO) also mainly afforded **4** (Entry 6). Interestingly, however, the reaction of sulfone **1g** (X = SO$_2$) gave only **3** (Entry 7). These results apparently indicate that the lone pair of sulfur traps the Pd catalyst, leading to intermolecular catalyst transfer. The different behavior of N and O in the second period and S in the third period might be accounted for by strong interaction between the soft lone pair of sulfur and soft Pd with a large atomic radius. In order to confirm that sulfide linkage interferes with intramolecular catalyst transfer, we conducted the reaction of dibromophenylene **6** with phenylboronicacid ester **7** in the absence or presence of diphenyl sulfide (Scheme 3). When the reaction was carried out in the absence of diphenyl sulfide, only phenyl-disubstituted phenylene **8** was obtained, indicating that intramolecular catalyst transfer took place on **6**. On the other hand, the reaction of **6** with **7** in the presence of diphenyl sulfide equimolar to **6** afforded **8** and monosubstituted **9** in the ratio of 56/44. This indicates that diphenyl sulfide can trap the Pd catalyst during transfer on the benzene ring of **6**, resulting in intermolecular catalyst transfer.

Since we found that ^{t}Bu$_3$PPd undergoes intramolecular transfer on several functional groups, we applied this chemistry to Suzuki-Miyaura unstoichiometric polycondensation of 1.3 equivalent of **1** and 1.0 equivalent of phenylenedibronic acid **5** in the presence of ^{t}Bu$_3$PPd G2 precatalyst (Scheme 2, Table 2). Intramolecular catalyst transfer on **1** is expected to afford high-molecular-weight polymer with boronic acid moieties at both ends even if excess **1** is used, as in the case of unstoichiometric Suzuki-Miyaura polycondensation of aromatic monomers.[13a] Indeed, polycondensation using **1a**-**d**, and **1g**, which exhibited intramolecular catalyst transfer in the reaction with **2** (Table 1), afforded high-molecular-weight polymer (M_n ≥ 7500) (Table 2, Entries 1-4, and 7), and the polymer obtained in the initial stage appeared to have boronic acid moieties at both ends (Figure S12, S14, S17, and S20), although the polymer formed from **1g** and **5** did not show any peaks in the MALDI-TOF mass spectrum. In contrast to these cases, polycondensation using **1e** and **1f**, which induced intermolecular catalyst transfer in the reaction with **2**



In the absence of diphenyl sulfide: **8**/**9** = 100/0
In the presenceof diphenyl sulfide: **8**/**9** = 56/44

Scheme 3. Effect of diphenyl sulfide additive on Suzuki-Miyaura coupling reaction of **6** with **7** in the presence of ^{t}Bu$_3$PPd.

(Table 1), resulted in the formation of low-molecular-weight polymer (Entries 5 and 6), probably through normal unstoichiometric polycondensation, in which the polymer ends are capped with excess monomers.

It should be noted that the MALDI-TOF mass spectra of the final products from **1a**, **c**, and **d** with **5** showed a single series of peaks due to cyclic polymers (Figure S11, S16, and S19); unfortunately we could not obtain spectra from the final products of the reactions of **1b** and **g** with **5**. Formation of cyclic polymer in polycondensation is not unusual under stoichiometric conditions, whereas unstoichiometric polycondensation generally affords linear telechelic polymer with the same monomer units at both ends, irrespective of normal or abnormal reaction.[20] However, we have found that unstoichiometric Suzuki-Miyaura polycondensation of excess dibromoarylene and 1.0 equivalent of arylenediboronic acid (ester) catalyzed by ^{t}Bu$_3$PPd selectively affords cyclic polymer when at least one of the two monomers has a kinked structure, such as in the case of *m*-phenylene.[14] Production of cyclic polymers in similar ^{t}Bu$_3$PPd-catalyzed polycondensation of **1a**, **c**, and **d** with **5**, which has a *p*-phenylene structure, implies that **1a**, **c**, and **d** act as monomers with kinked structure due to the presence of the sp^3 X groups (CH$_2$, N-Bu, and O).

Table 2. Unstoichiometric Suzuki-Miyaura polycondensation of **1** and **5** in the presence of ^{t}Bu$_3$PPd G2 precatalyst.[a]

Entry	**1**	M$_n$[b]	M$_w$/M$_n$[b]
1	**1a**	10400	4.37
2	**1b**	24900	3.91
3	**1c**	15500	5.14
4	**1d**	20500	2.69
5	**1e**	2400	1.46
6	**1f**	2960	1.42
7	**1g**	7500	4.14

[a] Polymerization of 1.3 equivalent of **1** and 1.0 equivalent of **5** was carried out with ^{t}Bu$_3$PPd G2 precatalyst in the presence of CsF (4.0 equivalent) and 18-crown-6 (8.0 equivalent) in THF ([**5**]$_0$ = 16.6 mM) and H$_2$O (THF/H$_2$O = 3.0/0.1) at room temperature for 24 h. [b] Estimated by GPC based on polystyrene standards (eluent: CHCl$_3$).

In conclusion, we have demonstrated that ^{t}Bu$_3$PPd undergoes intramolecular catalyst transfer not only on aromatic rings, but also through CH$_2$, CO, N-R, O, SO$_2$ located between benzene rings in the ^{t}Bu$_3$PPd-catalyzed Suzuki-Miyaura coupling reaction of dibromo compounds **1** having these functional groups with arylboronic acid **2**. On the other hand, the presence of S and SO in **1** induced intermolecular catalyst transfer, implying that the soft lone pair on sulfur traps the soft Pd catalyst during intramolecular catalyst transfer. Taking advantage of these findings, we conducted unstoichiometric Suzuki-Miyaura polycondensation of 1.3 equivalent of **1** bearing CH$_2$, CO, N-R, O, and SO$_2$ groups with 1.0 equivalent of *p*-phenylenediboroinic acid **5** in the presence of ^{t}Bu$_3$PPd G2 precatalyst, obtaining high-molecular-weight polymer with M_n 7500-24900 in spite of the use of excess **1**. Furthermore, the obtained polymers containing CH$_2$, N-R, and O linkages turned out to be cyclic, based on MALDI-TOF analysis. Intramolecular catalyst transfer on functional groups should make it possible to conduct CTCP of AB-type monomers containing these functional groups, providing access to well-defined engineering plastics, as well as to block copolymers consisting of engineering plastics and π-conjugated polymers. Further studies are in progress along this line.

Acknowledgements

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Keywords: catalyst transfer • Suzuki-Miyaura coupling reaction • Pd catalyst • unstoichiometric polycondensation • cyclic polymer

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[19] It was confirmed that the reaction of **4e** with **2** proceeded much slower than the reaction of **1e** with **2** in the reaction of **1e** with 2 equivalent of **2** (Supporting Information 4-10, Table S3).

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Entry for the Table of Contents (Please choose one layout)

Layout 1:

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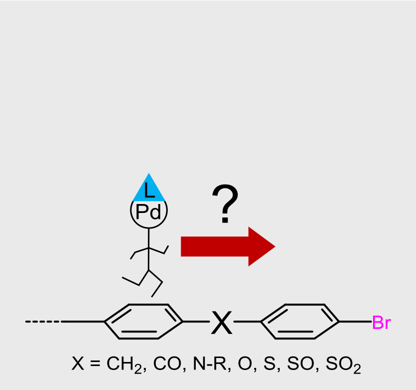
${}^{t}Bu_3PPd$ undergoes intramolecular catalyst transfer not only on aromatic rings, but also through CH_2, CO, N-R, O, SO_2 located between benzene rings in the ${}^{t}Bu_3PPd$-catalyzed Suzuki-Miyaura coupling reaction of dibromo compounds having these functional groups with arylboronic acid. On the other hand, the presence of S and SO in the dibromides induced intermolecular catalyst transfer.



Tsutomu Yokozawa, Natsumi Harada, Hajime Sugita, Yoshihiro Ohta*

Page No. – Page No.

Intramolecular Catalyst Transfer on a Variety of Functional Groups between Benzene Rings in Suzuki-Miyaura Coupling Reaction

Layout 2:

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Page No. – Page No.

Title

Text for Table of Contents