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COMMUNICATION

Chloride-promoted Pd-catalyzed direct C-H arylation for highly efficient phosphine-free synthesis of π-conjugated polymers

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

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We have successfully demonstrated a chloride-promoted Pd-catalyzed phosphine-free direct C-H arylation for highly efficient synthesis of high molecular weight π-conjugated polymers. Among halide ions, chloride ion played a crucial role for highly efficient C-H activation.

Palladium-catalyzed carbon-carbon (C-C) cross-coupling reactions are among the most important methods in modern organic chemistry.[1-4] A number of C-C bond formations rely on metal-catalyzed coupling reactions such as Suzuki-Miyaura[1], Stille[2], Negishi[3], and Kumada[4] processes. Many of organic materials based on π-conjugated frameworks have been synthesized by these palladium-catalyzed cross-coupling reactions.[5] Drawbacks of these reactions are, however, the use of various organometallic reagents as coupling partners. Synthesis of these reagents requires multi-step reactions. The cross-coupling reactions using these organometallic reagents produce stoichiometric amounts of metallic by-products. Less stability of borylated compounds for Suzuki-Miyaura cross-coupling[6] and toxic stannylated compounds for Stille cross-coupling discourage us from using such cross-coupling reactions. Direct (C-H) arylation has therefore attracted considerable attention as an alternative C-C coupling reaction in recent years.[7] Direct arylation has received increasing attention as a new synthetic method for π-conjugated polymers.[8]

Pd(II) salts are generally used for Pd(0) precursors in direct arylation.[8,9] Among the Pd(II) salts, $Pd(OAc)_2$ is generally used as the best precatalyst, because it is commercially available, relatively inexpensive, stable in air, and soluble in both water and organic solvents.[10] On the other hand, we have recently developed a regioselective direct arylation polycondensation of β-unprotected thiophenes by using stable and low cost carbon-supported Pd catalyst.[11] $PdCl_2$ is also a stable and low cost Pd(II) compound, but its solubility is not high in organic solvents.[10] Pd-catalyzed Heck-type C-H activation reactions conducted in the presence of $PdCl_2$ are known to be highly efficient. This is thought to be the existence of active and stable Pd complexes in the reaction media.[12] The chloride ion liberated from $PdCl_2$ may enhance the catalytic activity and stability. Nevertheless, $PdCl_2$ has not been recognized as an effective precatalyst for the direct arylation reactions and polymerizations. Thus, we expected that the chloride ion would play a key role to accelerate the direct arylation reaction (polycondensation).

In this communication, we report a chloride-promoted direct arylation reaction (polycondensation) of (hetero)aryl compounds such as 3,4-ehtylenedioxythiophene, **EDOT**, and fluoroarenes. In previous reports, the direct arylation polycondensation of **EDOT**, a building block for high performance device materials, with 2,7-dibromo-9,9-dioctylfluorene, **F8**, gave high molecular weight (M_n = ca. 40000) poly([3,4-dioxyethylenethiophene-2,5-diyl]-*alt*-[9,9-dioctylfluorene-2,7-diyl]), **PEDOTF8**, under the optimized phosphine-free conditions (2.0 mol% of $Pd(OAc)_2$, 30 mol% of 1-adamantanecarboxylic acid [1AdCOOH], 2.5 equivalent of K_2CO_3, in *N,N*-dimethylacetoamide [DMAc], 100°C, 6 h).[9c] In contrast to the heating conditions, microwave-assisted heating conditions (1.0 mol% of $Pd(OAc)_2$, 2.5 equivalent of potassium pivalate, in DMAc, 0.5 h) enhanced the efficiency of the polycondensation with **EDOT** to give higher molecular weight polymer **PEDOTF8** (M_n = 77000[13]).[9d]

To begin on the investigation of chloride-promoted direct arylation, the polycondensation of **EDOT** with **F8** was carried out without or with halide additives (2.0 mol%) under the following conditions: 30 mol% of 1AdCOOH[9c], 3.0 equivalent of K_2CO_3, and 1.0 mol% of palladium in DMAc (Scheme 1). The reaction mixture was filtered and poured into methanol, giving **PEDOTF8**. All the ^{1}H NMR signals of the obtained **PEDOTF8** could be assigned to the protons of the repeating unit, and a signal of the terminal EDOT unit was observed (Fig. S1).

To explore the suitable heating conditions for the direct arylation polycondensation with **EDOT**, we first tested $Pd(OAc)_2$ as a precatalyst, which is usually used in direct arylation with thiophenes.[9] The polycondensation was carried out at various temperatures (80-120 °C) for 15 min (Fig. 1a). The M_n value of **PEDOTF8** obtained at 80 °C was not high (M_n =1800, M_w/M_n = 1.39), but the M_n value increased as the temperature rose (Fig. 1a, red line). The direct arylation polycondensation at 120 °C gave **PEDOTF8** with M_n = 6600 (M_w/M_n = 2.47) in good yield (82%). $PdCl_2$ was next tested as a precatalyst. Remarkably, $PdCl_2$ was much more efficient than $Pd(OAc)_2$ in the direct arylation polycondensation with **EDOT**. The M_n values and the yields of **PEDOTF8** markedly increased in proportion as the temperature rose

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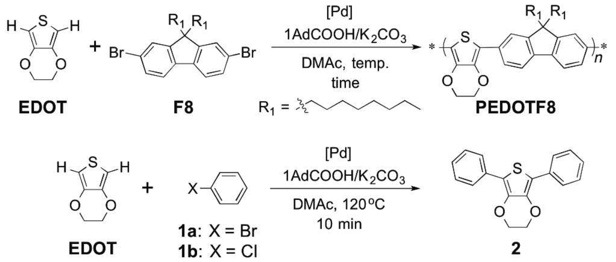
† Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

(Fig. 1a, blue line). The M_n value of **PEDOTF8** reached up to 40000 (M_w/M_n = 2.83) when the polycondensation was carried out at 120 ^{o}C. We found that PdCl$_2$ is capable of accelerating the direct arylation polycondensation of **EDOT** with **F8**, giving high molecular weight **PEDOTF8** in high yield (97%).



Scheme 1 Direct arylation of **EDOT**.

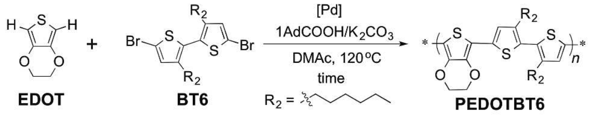
To clarify the difference between PdCl$_2$ and Pd(OAc)$_2$ for the polycondensation efficiency, the relationship between M_n and reaction time was examined. The M_n value of **PEDOTF8** increased to 48000 until 60 min, when the polycondensation was carried out using Pd(OAc)$_2$ (Fig. 1b, red line), but the M_n value did not increase after 60 min. On the other hand, the use of PdCl$_2$ showed a significant increase of M_n value (Fig. 1b, blue line) with time. The M_n value of **PEDOTF8** reached to 80000 (M_w/M_n = 4.09), which is about twice as high as the M_n value obtained by the polycondensation using Pd(OAc)$_2$. These results imply that the palladium active species derived from PdCl$_2$ were not deactivated. The highly efficient direct arylation polycondensation is probably caused by the existence of chloride ions.

Fig. 1c summarizes the results of the direct arylation polycondensation using Pd(OAc)$_2$ in the presence of additives as halogen sources. 2.0 mol% of *n*-tetrabutylammonium halides (^{n}Bu$_4$NX) was added to the Pd-catalyzed reaction system using Pd(OAc)$_2$. The direct arylation with ^{n}Bu$_4$NF, ^{n}Bu$_4$NCl, and ^{n}Bu$_4$NBr afforded **PEDOTF8** with high M_n values compared with that without these additives. Fluoride and bromide as well as chloride accelerated the direct arylation. On the other hand, ^{n}Bu$_4$NI was not effective, giving the polymer with low M_n value.

The dependence of M_n values of **PEDOTF8** on the polymerization time was examined in both "PdCl$_2$" and "Pd(OAc)$_2$ + ^{n}Bu$_4$NCl" systems (Fig. 1d). PdCl$_2$ precatalyst showed a higher accelerating effect than "Pd(OAc)$_2$ + ^{n}Bu$_4$NCl". The direct arylation using "Pd(OAc)$_2$ + ^{n}Bu$_4$NCl" system for 120 min gave high molecular weight **PEDOTF8** (M_n = 70200, M_w/M_n = 3.60), but did not amount to the M_n value obtained by the polycondensation using PdCl$_2$ (M_n = 80000, M_w/M_n = 4.09). The molecular weight (M_n) of the polymer afforded by the polycondensation using Pd(OAc)$_2$ was less than 50000, which indicates the propagation terminated after about 60 min (Fig. 1b). On the other hand, the polymerization was rapidly propagated by both PdCl$_2$ and "Pd(OAc)$_2$ + ^{n}Bu$_4$NCl" systems until 30-60 min and continued after 60 min (Fig. 1d). These two similar curves suggest that the chloride promoted the direct arylation polycondensation and suppressed the deactivation of the palladium catalyst. The chloride may behave as a ligand for stabilizing Pd species under the direct arylation conditions.

The efficiency of the chloride-promoted direct arylation was also confirmed by the reaction of **EDOT** with bromobenzene, **1a** (Scheme 1, Table S2). The reaction with Pd(OAc)$_2$ gave 2,5-diphenyl EDOT, **2**, in 64% yield. On the other hand, the yield of **2** was significantly increased to 97% by using PdCl$_2$ precatalyst. The direct arylation using Pd(OAc)$_2$ and ^{n}Bu$_4$NCl also gave a high yield of **2** (93%). The catalytic activity for the direct arylation polycondensation was the following order: PdCl$_2$ > "Pd(OAc)$_2$ + ^{n}Bu$_4$NCl" > Pd(OAc)$_2$.

To synthesize other EDOT-based π-conjugated polymers by the direct arylation polycondensation of **EDOT**, with 5,5'-dibromo-3,3'-dihexyl-2,2'-bithiophene, **BT6**, was used as a monomer. The polycondensation was carried out at 120 ^{o}C for 15 min in DMAc under the following conditions: 1.0 mol% of PdCl$_2$, 30 mol% of 1AdCOOH, and 3.0 equivalent of K$_2$CO$_3$. The expected poly([3,4-dioxyethylenethiophene-2,5-diyl]-*alt*-[3,3'-dihexyl-2,2'-bithiophene-5,5'-diyl]), **PEDOTBT6**, with high molecular weight (M_n = 36000, M_w/M_n = 6.15) could be obtained in 95% yield (Scheme 2). On the other hand, the polycondensation using Pd(OAc)$_2$ gave lower molecular weight **PEDOTBT6** (M_n = 22000, M_w/M_n = 17.04) in 73% yield.



Scheme 2 Chloride-promoted direct arylation polycondensation of **EDOT** with **BT6**.

To investigate the effect of counter anions of the Pd(II) species on the redox properties, cyclic voltammetry (CV) of PdCl$_2$, Pd(OAc)$_2$ and "Pd(OAc)$_2$ + ^{n}Bu$_4$NCl" was performed in Et$_4$NBF$_4$/DMAc solution (Fig. 1e). An irreversible reduction peak (E_R) from Pd(II) to Pd(0) was observed in each case. The E_R value (-1.01 V vs. Ag/AgCl) of PdCl$_2$ was lower than that (-1.56 V vs. Ag/AgCl) of Pd(OAc)$_2$. Thus, PdCl$_2$ has an electron-deficient property compared with Pd(OAc)$_2$. The E_R value slightly reduced from -1.56 V to -1.47 V when 2.0 equivalent of ^{n}Bu$_4$NCl was added to the Pd(OAc)$_2$ / DMAc solution. After heating the solution of Pd(OAc)$_2$ and ^{n}Bu$_4$NCl at 120 ^{o}C for ca. 1 min, the E_R value (-1.14 V vs. Ag/AgCl) approached the E_R value of PdCl$_2$. UV-vis absorption spectra were measured in DMAc solution (Fig. 1f). PdCl$_2$ showed a charge transfer absorption band around 410-580 nm. On the other hand, Pd(OAc)$_2$ showed a band at 380-500 nm. This band was shifted to a lower energy region when 2.0 equivalent of ^{n}Bu$_4$NCl was added to the Pd(OAc)$_2$ / DMAc solution. Moreover, the absorption band was slightly red-shifted by heating the solution. The chloride ions affected the reduction potential and the optical property of Pd(II) as well as the catalytic activity of the palladium complex. The plausible mechanism is the concerted metalation-deprotonation (CMD) [14] proposed for the Pd-catalyzed direct arylation (Scheme S1). The direct arylation polycondensation of **EDOT** with **F8** in the lack of carboxylate additives did not give the polymer (Table S3, entries 1 and 2). These results support the CMD mechanism. To clear the effect of chloride, the polycondensation with 1.0 mol% of PdCl$_2$ was carried out in the presence of AgNO$_3$ as a chloride scavenger. The polycondensation with 2.0 mol% of AgNO$_3$ gave the low molecular weight polymer (M_n = 8600, M_w/M_n = 2.13) in 78% yield (entry 3). The chloride scavenger decreased the reaction efficiency. Moreover, the excess amount of AgNO$_3$ did not give the polymeric products (entry 4 and 5). It is known that silver salt ($AgCO_3$ or $AgNO_3$ + K_2CO_3) plays an agent for the abstraction of halide ions from halopalladium species to generate reactive palladium species for some reactions [15]. However, the excess chloride scavengers inhibited the direct arylation. These results suggested that the halide ion plays a good ligand for a cationic Pd(II) species and prevents the Pd catalyst from forming an inactive Pd species. Similar to the common phosphine ligands [16-18], the weak but moderately donating nature of the chloride (or bromide) ligand would tune Pd(II) to the suitable cationic Pd character for moving from the intermediate **B** to **C** in the reaction (Scheme S1).

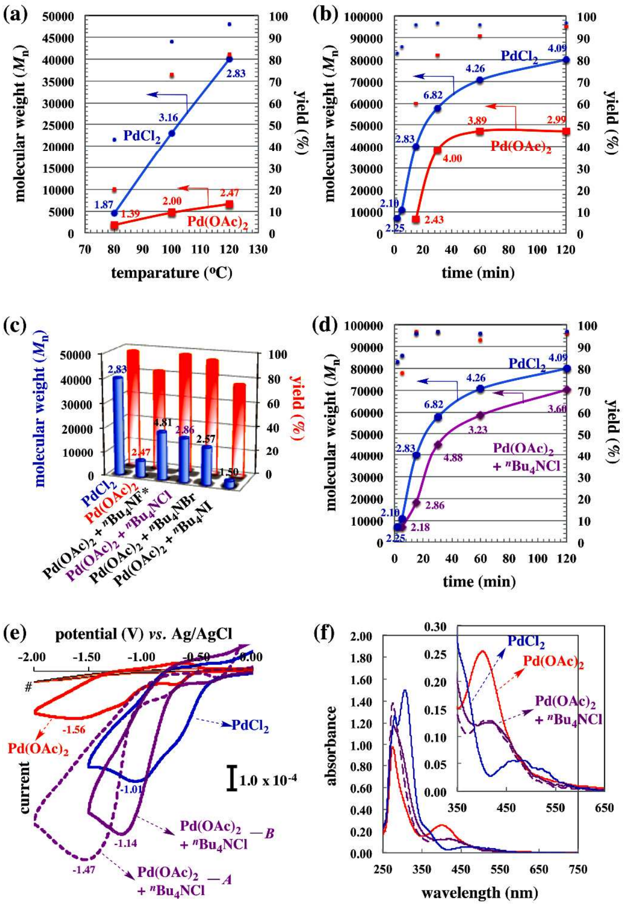
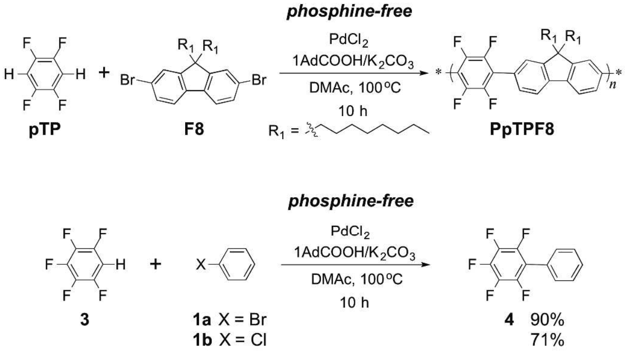


Fig. 1 (a)-(d) Results of the polycondensation of **EDOT** with **F8**. The value shown in figure is polydispersity (M_w/M_n). (a) Dependence of M_n value on temperature for 15 min. (b) Dependence of M_n value on time at 120°C. (c) Results of the direct arylation polycondensation with various additives at 120°C for 15 min. * ^{n}Bu$_4$NF was added as 1.0 M THF solution. (d) Dependence of M_n value on time at 120°C. **Conditions**: **EDOT** (0.30 mmol), **F8** (0.30 mmol), [Pd] (1.0 mol%), ^{n}Bu$_4$NX (0.0 or 2.0 mol%), 1AdCOOH (30 mol%), K_2CO_3 (3.0 mmol), DMAc (1.0 mL), 80-120°C, under argon. (e) Cyclic volammograms of palladium under polycondensation conditions. **Conditions**: In 0.1 M Et_4NBF_4/DMAc; Pt counter electrode, Pt working electrode, Ag/AgCl reference electrode; scan rate, 0.1 V/sec; Fe/Fe$^+$ = 0.41 V. # Back ground. (f) UV-vis absorption spectra of various palladium in DMAc. red line: $PdCl_2$, blue line: $Pd(OAc)_2$, purple dotted line: $Pd(OAc)_2$ + ^{n}Bu$_4$NCl before heating, purple solid line: $Pd(OAc)_2$ + ^{n}Bu$_4$NCl after heating.

Generally, palladium-catalyzed direct arylations proceed efficiently by use of phosphine ligands, but many of phosphine ligands have some drawbacks such as high cost, poor thermal and air stability. The side reaction involving phosphine ligands has also been reported.[16] Fluoroarenes as well as **EDOT** can also be used as substrates for direct arylation reaction.[16-18] However, it is known that the reaction of **F8** with fluoroarenes requires phosphine ligands. Thus, the direct arylation polycondensation of 1,2,4,5-tetrafluorobenzene, **pTP**, with **F8** yielded poly([2,3,5,6-tetrafluoro-1,4-phenylene]-*alt*-[9,9-dioctylfluorene-2,7-diyl]), **PpTPF8**, under both Kanbara's conditions (5.0 mol% of $Pd(OAc)_2$, 10 mol% of ^{t}Bu$_2$MePHBF$_4$, 2.0 equivalent of K_2CO_3, in DMAc, 100°C, 24 h) [18] and Ozawa's conditions (0.5 mol% of $Pd_2(dba)_3$-$CHCl_3$, 2.0 mol% of $P(C_6H_4$-*o*-$OMe)_3$, 1.0 equivalent of pivalic acid, 3.0 equivalent of Cs_2CO_3, in THF, 100°C, 24 h)[16], respectively. Thus, we attempted to apply our chloride-promoted polymerization to the phosphine-free direct arylation of fluoroarenes. The direct arylation polycondensation of **pTP** with **F8** in the absence of phosphine ligand was carried out at 100°C in DMAc by using 30 mol% of 1AdCOOH, 3.0 equivalent of K_2CO_3, and 1.0 mol% of $PdCl_2$, giving **PpTPF8** with high molecular weight (M_n = 21000, M_w/M_n = 6.77) in high yield (86 %). On the other hand, the phosphine-free direct arylation polycondensation using other catalysts such as $Pd(OAc)_2$ and $Pd(CF_3COO)_2$ did not give the polymer as previously reported (Table S4).[16,18] The structure of **PpTPF8** was confirmed by the ^{1}H NMR spectrum (Fig. S5), which was in good agreement with that of previously reported **PpTPF8** [16,18]. The tetrafluorophenylene end unit appeared at ca. 7.1 ppm. The fluorine signals derived from the repeating and end units of the alternating copolymer, **PpTPF8**, were observed in the ^{19}F NMR spectrum (Fig. S6). Similarly, the efficient phosphine-free direct arylation of pentafluorobenzene, **3**, with **1a** or **1b** was achieved to give 1,2,3,4,5-pentafluorobiphenyl, **4**, in high yield (Scheme 3, Table S5). It is noteworthy that chlorobenzene could be used as an effective reactant under the conditions.



Scheme 3 Chloride-promoted phosphine-free direct arylation of fluoroarenes.

In conclusion, chloride ion played a key role to significantly increase the catalytic reactivity and stability of Pd species for direct arylation, achieving a highly efficient phosphine-free direct arylation synthesis of π-conjugated polymers.

Acknowledgements

This work was supported by Grant-in-aid for Young Scientists (B) 15K17872 and Scientific Research (C) 26410141 for financial support. We thank Prof. Dr. Shinsuke Inagi in Tokyo Institute of Technology for ^{19}F NMR measurements.

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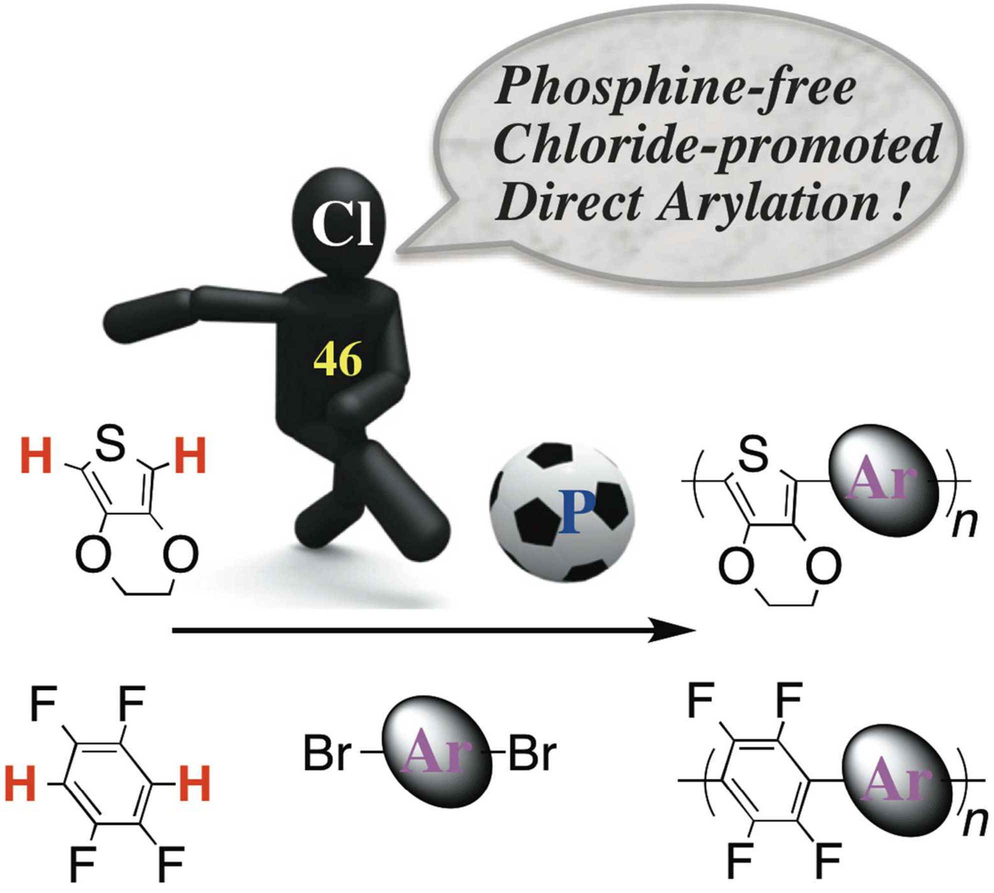
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