

論文の内容の要旨

Iron-Catalyzed C–H/C–H Coupling for Synthesis of Functional Small Molecules and Polymers

(鉄触媒 C–H/C–H カップリングによる
機能性低分子及び高分子の合成)

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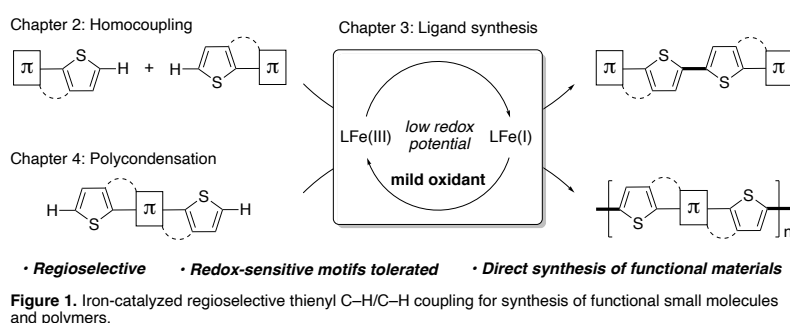
1. Introduction

Conjugated compounds containing C(sp²)–C(sp²) linkages are one of the most important classes of compounds because of the interaction of their *p*-orbitals with electrons and photons. Therefore, development of C(sp²)–C(sp²) bond-forming reactions is an important subject in organic chemistry. To this end, transition-metal-catalyzed C(sp²)–H/C(sp²)–H coupling has been extensively studied in the past decade as one of the most straightforward methods to construct a C(sp²)–C(sp²) bond.¹ However, these reactions require strongly oxidizing conditions to turn over the catalytic cycle with a large redox potential [e.g. E° (Pd^{II}/Pd⁰) = + 0.915 V vs NHE], which cause undesired oxidation of products or unwanted side reactions.² This situation makes it difficult to apply this attractive transformation to the synthesis of redox-sensitive π -materials of importance in materials science. To solve this problem, I focused on the reactivity of iron: low redox potential [E° (Fe^{III}/Fe^I) < + 0.55 V vs NHE], which enables mild catalytic cycle using mild oxidant,³ and C–H activation through σ -bond metathesis mechanism, which enables regioselective C–H activation by acidity control (as revealed by my master course studies).⁴

To this end, I first investigated the iron catalytic system that catalyzes regioselective C–H/C–H homocoupling of thiophene compounds and determined that oxalate serves as a mild oxidant in combination with AlMe₃ base and a tridentate phosphine ligand. Then, a modular synthetic method of a tridentate phosphine ligand was developed to further accelerate the exploration of this reaction system. To expand the applicability of iron-catalyzed regioselective thienyl C–H/C–H coupling to the synthesis of polymeric compounds, iron-catalyzed regioselective thienyl C–H/C–H polycondensation was developed by suppressing catalyst deactivation by ligand design. The obtained polymer was

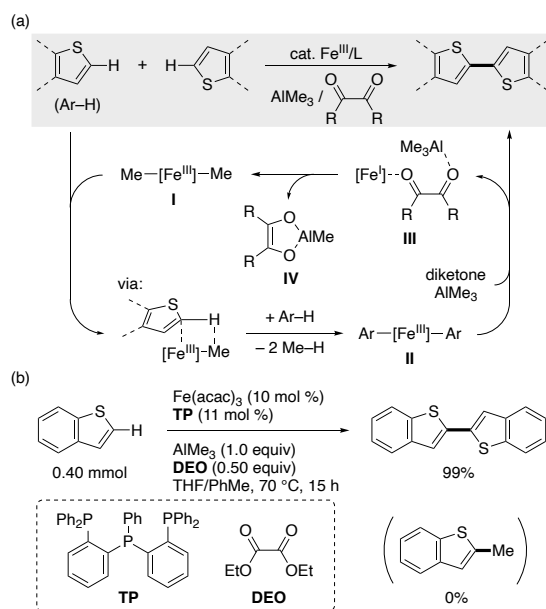
applied as a hole transporting material for perovskite solar cells to demonstrate the practicability of this method. The reactions described herein highlight the potential of iron, the most

abundant transition-metal on earth, for the direct synthesis of functional small molecules and polymers of importance in materials science.



2. Iron-catalyzed regioselective thienyl C–H/C–H homocoupling

Conjugated bithiophene compounds have wide application in organic devices. These compounds are highly redox-sensitive, requiring a mild two electron acceptor for thienyl C–H/C–H coupling. Taking advantage of the low redox potential of iron and regioselective C–H activation through σ -bond metathesis, I envisioned that the reaction system using Fe(III) as a catalyst, tridentate phosphine as a ligand, AlMe₃ as a base, and dichloroalkane as an oxidant⁵ would be desirable for regioselective thienyl C–H/C–H homocoupling. When benzo[*b*]thiophene was subjected to this reaction condition, the homocoupling product was obtained in no higher than 50% yield due to the catalyst inhibition by alkene generated upon reduction of



dichloroalkane. Seeking for a mild oxidant that does not generate alkene, I came up with the idea of using diketone as a mild oxidant based on the fact that a carbonyl group can serve as a directing group for iron-catalyzed C–H activation. As shown in Figure 2a, diketone in combination with Al(III) regenerates a Fe(III) catalyst (**I**) via inner-sphere electron transfer (**III**) to form an aluminum enediolate (**IV**). The strong oxophilicity of Al(III) contributes as the driving force for effective catalyst turnover. Based on this hypothesis, diethyl oxalate (**DEO**) was determined to be an excellent oxidant. This reaction takes place exclusively at the C–H bond next to the sulfur atom of a thienyl group and C–H methylation does not take place (Figure 2b). This reaction tolerates various kinds of redox-sensitive π -motifs widely used in organic electronics due to the mildness of oxalate. The results of stoichiometric experiments indicated that the C–H bond of a thiophene is activated by methyliron species through a σ -bond metathesis mechanism. KIE experiment suggested that neither of the C–H activation steps is the turnover-limiting step and therefore the catalyst regeneration step is the turnover-limiting step.

3. Development of a synthetic method for tridentate phosphine ligands

To further accelerate the investigation of Fe(III)/TP/AlMe₃/DEO system, a practical method to synthesize derivatives of TP is desirable. Previously, the ligand synthesis required dichloroarylphosphines that are toxic, moisture sensitive, and difficult to purify. In this work, I developed a simple and scalable method to synthesize derivatives of TP by sequential addition of organolithium reagents to P(OPh)₃.

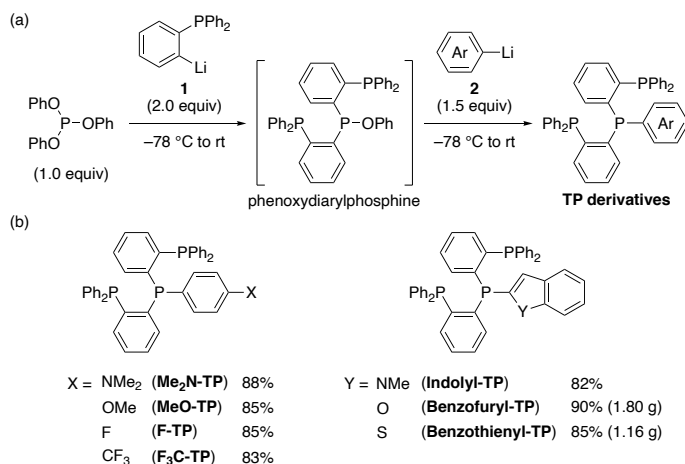


Figure 3. Synthesis of TP derivatives. (a) Sequential addition of organolithium reagents to P(OPh)₃. (b) Substrate scope.

First, 2.0 equiv of (2-(diphenylphosphanyl)phenyl)lithium (**1**) was reacted with 1.0 equiv of P(OPh)₃ (Figure 3a). Then the crude reaction mixture was reacted with 1.5 equiv of aryllithium (**2**). Finally, the pure products were easily obtained by recrystallization. This method facilitates the synthesis of tridentate phosphine ligands possessing various kinds of substituents on the central phosphine ranging from substituted phenyl groups to heteroaryl groups (Figure 3b) even on a gram scale. Single crystal X-ray analysis explicitly confirmed the structure of a tridentate phosphine ligand having a benzofuryl group as a central aryl group.

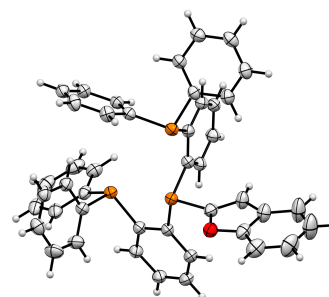


Figure 4. ORTEP drawing of benzofuryl-TP. Thermal ellipsoids are shown at 30% probability.

4. Iron-catalyzed regioselective thienyl C–H/C–H polycondensation

Currently, conjugated polymers are mainly synthesized by transition-metal-catalyzed cross-coupling of a C–X (X: (pseudo)halide) bond and a C–M (M: metal) bond. However, these bonds need to be preinstalled to the monomer and removed from the polymer, which requires additional synthetic steps. Therefore, transition-metal-catalyzed C–H/C–H polycondensation is recognized as an ideal polymerization method. The biggest challenge is that it requires extremely high catalytic activity to achieve efficient polymerization. In this work, I achieved iron-catalyzed regioselective thienyl C–H/C–H polycondensation by improving the efficiency of the homocoupling reaction by suppression of catalyst deactivation. To understand the catalyst deactivation pathway, I recovered the ligand from the crude reaction mixture and analyzed by HRSM. Interestingly, methylation of the ligand was observed. This result suggests that *ortho* C–H methylation of the ligand deactivates the catalyst by creating sterics around the catalyst center. To suppress the intramolecular *ortho* C–H activation of the ligand, I designed heteroaryl-TP possessing heteroaryl group on the central phosphine. Based on this hypothesis, heteroaryl-TPs were synthesized by the method described above and used for polycondensation. As shown in Figure 5a, the polymer length was doubled by using **benzofuryl-TP**

compared to **TP**. With optimal ligand in hand, redox-sensitive homopolymers and copolymers containing conjugated and electron-rich structures were obtained with DP up to 46 with a unimodal distribution owing to the effectiveness of iron catalytic cycle and the mildness of oxidant. M_w/M_n value of around 2 indicated that this polymerization reaction takes place through step-growth mechanism because of the weak interaction of Fe(III) with the polymer's π surface. The reaction took place exclusively at the C–H bond next to the sulfur atom of the thienyl group and no polymer branching was observed as judged by NMR spectra. Also, the residual iron was removed to less than 40 ppm by post treatment of the polymer with thiol-functionalized silica scavenger. Finally, a hybrid polymer of PTAA and P3HT (**Mes-TADHT**) was synthesized by this method and used as a hole-transporting material for a normal structure MAPbI₃ solar cell. The devices fabricated in collaboration with Dr. Lin in Matsuo Lab achieved high efficiency over 21% and stability over 1 month (Figure 5b).

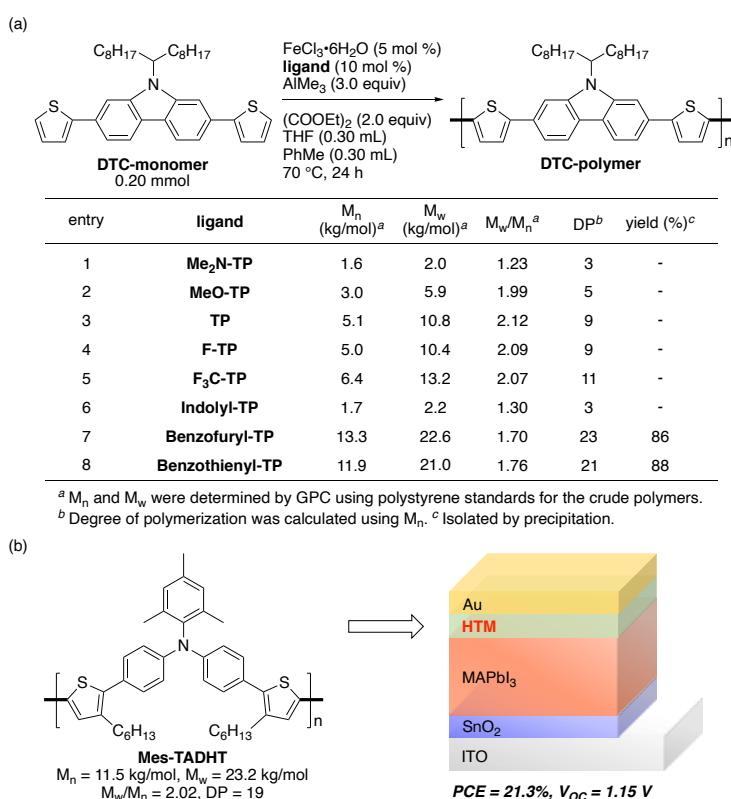


Figure 5. Iron-catalyzed regioselective thienyl C–H polymerization. (a) Effect of ligand on polymer length. (b) Application to perovskite solar cell.

5. Conclusion

In summary, I developed iron-catalyzed thienyl C–H/C–H homocoupling and polycondensation using tridentate phosphine ligands and oxalates as key enablers. Tridentate phosphine ligand played a key role in controlling the reactivity of iron and oxalate served as a mild oxidant in combination with oxophilic Al(III). These reactions gave direct access to conjugated and/or electron-rich thiophene compounds of interest in materials science. This work highlights the potential of using the two most abundant metals on earth, Fe and Al,⁶ for the synthesis of functional small molecules and polymers of importance in energy device applications.

6. References

- [1] Yang, Y. *et al. Chem. Rev.* **2017**, *117*, 8787. [2] Grzybowski, M. *et al. Angew. Chem. Int. Ed.* **2013**, *52*, 9900. [3] Shang, R. *et al. Chem. Rev.* **2017**, *117*, 9086. [4] Doba, T. *et al. Nat. Catal.* **2019**, *2*, 400. [5] Shang R. *et al. J. Am. Chem. Soc.* **2016**, *138*, 10132. [6] Nakamura, E. *et al. Nat. Mater.* **2011**, *10*, 158.