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Perfluorocyclopentadienyl Radical Derivative as an Organocatalyst for Oxidative Coupling of Aryl- and Thienylmagnesium Compounds under Atmospheric Oxygen

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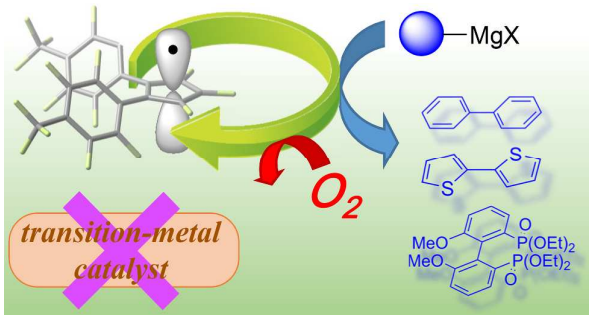
Abstract: The oxidative homo-coupling reaction of Grignard reagents in the presence of atmospheric oxygen molecules proceeded in the presence of heptafluorotolyl-substituted perfluorocyclopentadienyl radical. The turnover number (TON) was over 30 for the coupling reactions of PhMgBr to give biphenyl. The organocatalyst could couple thienylmagnesium compounds to give bithiophene derivatives in up to 94% yield. Furthermore, gram-scale synthesis of 6,6'-dimethoxybiphenyl-2,2'-diyl-bis(phosphonic acid diethyl ester) was demonstrated. Stabilization of the phenyl radical for the inhibition of the side-reaction was also considered using DFT calculations.



The C-C coupling reactions were largely developed using transition-metal catalysts such as the Pd-catalyzed Suzuki-Miyaura coupling. On the other hand, transition metal-free oxidative coupling reactions were reported using stoichiometric non-metal oxidants.[1] Recently, organocatalyst-catalyzed oxidative homo-coupling reactions of Grignard reagents in the presence of molecular oxygen were reported.[2] Although the catalytic reaction is one of the most efficient methods for the synthesis of symmetrical biaryls,[3,4,5] only three examples using organocatalysts have been reported to date. The first and challenging example, used a TEMPO-catalyzed reaction, was reported by Studer et al. in 2008.[2a] Although the reaction of PhMgBr gave an 81% yield of biphenyl in the presence of 14 mol% TEMPO, several sequential reaction cycles (coupling reaction of PhMgBr by TEMPO → purging with O_2 for recycling TEMPO → addition of PhMgBr → •••) were required to inhibit the formation of phenol as a by-product. In 2015, we reported a four electron-accepting organic oxidant **1** that mediated the oxidative homo-coupling of Grignard reagents bearing aryl, alkenyl, or benzyl group stoichiometry.[2b] Furthermore, a catalytic reaction using 10 mol% of **1** was also demonstrated under dry-air conditions to give homo-coupling products with over 90% yields.[2b] The catalytic coupling reactions using **1** proceeded only by exposure to dry air under stirring except for the extra operation

in contrast to the report by Studer et al.[2a] In 2016, Amaya and Hirao et al. reported the same reactions using 15 mol% of *N*,*N*'-diphenyl-*p*-benzoquinonediimine catalyst to give 61%–85% coupling products.[2c] More recently, Matano et al. also reported the same reaction using 1 mol% of porphyrin derivative to give 31% coupling product.[2d] The role of oxygen molecules in all organocatalyst-catalyzed oxidative homo-coupling is the re-generation of the catalyst from its reduced form to turn over the catalytic cycle. However, an oxygen-molecule induced side reaction with the Grignard reagent that produced an oxide product, such as phenol from PhMgBr, inhibited the high yield of homo-coupling products.[2a] In contrast, the catalytic system using **1** forms only a trace amount of the by-product under atmospheric conditions, and high yields of the coupling products can be achieved as mentioned above.[2b] The mechanism of homo-coupling of Grignard reagents using **1** involves a) **1** mediated stoichiometric homo-coupling of four molar RMgX to give two moles of R-R and an anion species **2** derived from **1**, b) **2** converted to the perfluorocyclopentadienyl radical **3** in the presence of atmospheric oxygen, and **3** catalyzed the homo-coupling reaction of the rest of the RMgX to give R-R (Figure 1).[2b]

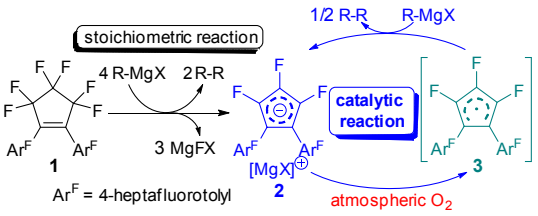


Figure 1 Mechanism of oxidative homo-coupling of RMgX using **1**.

Unfortunately, the active catalyst species **3** could not be isolated from the coupling reaction mixture.

If **3** can be used for the reaction directly, higher catalytic activity could be expected. In this study, an alternative synthesis of the active species **3** from **1** was performed, and its utilization for the oxidative coupling reaction was demonstrated.

Firstly, the generation of active species **3** was studied. Purified **1**[6] was converted to active species **3** by treatment with Mg; the oxidant **1** was treated with Mg turnings in the presence of trace I_2 in THF at 40°C for 4 h to give anion species **2**. It was readily converted to active species **3** under dry air. These species were confirmed by ^{19}F NMR or ESR analysis (Figure 2).[2b,7] Isolation of **3** was failed because **3** was decomposed by concentration of the THF solution.

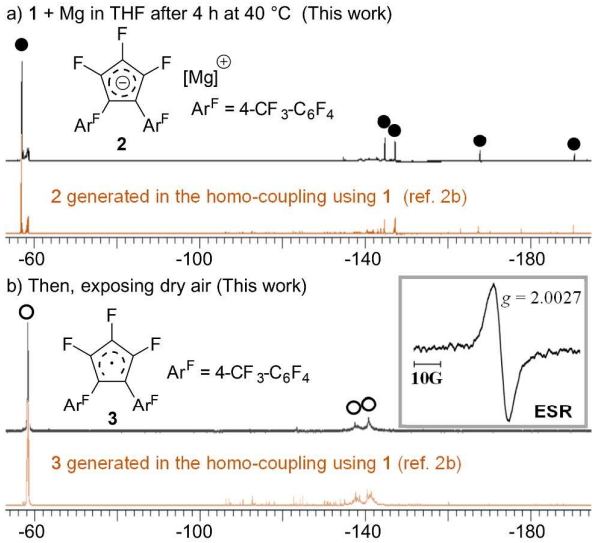
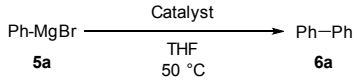


Figure 2 Confirmation of **2** and **3** by ^{19}F NMR and ESR.

The active species **3** was used for the oxidative homo-coupling of PhMgBr (**5a**). When the solvent effect was studied, the THF solvent gave the best result as with the cases using **1** (Table 1, entries 1, 3–5).[2b] However, the addition of triethylamine in the THF remarkably decreased the yield of biphenyl (**6a**) (entry 2). Because the catalyst **3** was not destroyed with triethylamine in THF, we assumed that the triethylamine altered the reactivity of **5**. The reaction using 10 mol% of **3** at 50°C for 6 h afforded **6a** in 98% yield (entry 6). When the catalyst loading was 5 mol% and 2 mol%, **6a** was obtained in 81% yield for 24 h and 62% yield for 3 days, respectively (entries 8, 10). Although the low catalyst loading of **3** gave a somewhat low yield compared to the reaction using **1** (entries 8, 10 vs. 9, 11), the turnover numbers (TON) were roughly similar. The TON in the cases of **1** could not be directly calculated from the catalyst loading. As described above, **1** initially acted as a stoichiometric oxidant and then as a catalyst in the form of **3**.[2b] For instance, in the case of the reaction using 10 mol% of **1** (Table 1, entry 7), 20% of **6a** was obtained through the stoichiometric reaction and 73% of **6a** was obtained through the catalytic reaction; TON = 7.3.[8] In contrast, the TON of the reaction using 10 mol% of catalyst **3** as a one-electron oxidant was calculated to be 9.8 (entry 6). When the catalyst loading was 10 mol%, the TON of **3** was slightly larger than that of **1**. In contrast, when the catalyst loading was 2 mol%, the TON of **3** was slightly lower than that of **1**. Comparison of the results of **1** and **3** showed that the catalytic activity of **3** did not exceed the reaction activity of **1** for initial stoichiometric coupling.

Table 1 Homo-coupling Reaction of PhMgBr (**5a**)[a]



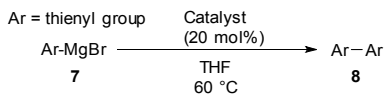
Entry	Catalyst (mol%)	Solvent	Time (h)	Yield (%)[b]	TON
1	**3** (5)	THF	6 h	62[c]	
2[d]	**3** (5)	THF	6 h	18[c]	
3	**3** (5)	CPME	6 h	51[c]	
4	**3** (5)	$(CH_2Cl)_2$	6 h	49[c]	
5	**3** (5)	toluene	6 h	34[c]	
6	**3** (10)	THF	6 h	98	9.8
7	**1** (10)	THF	6 h	93	7.3
8	**3** (5)	THF	24 h	81	16
9	**1** (5)	THF	24 h	87	15
10	**3** (2)	THF	3 days	62	31
11	**1** (2)	THF	3 days	76	36

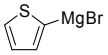
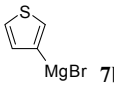
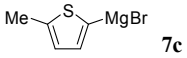
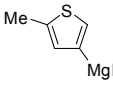
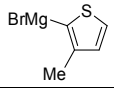
[a] The use of 1.0 mmol of **5a** (1.0 M THF solution, which was titrated with 1,10-phenanthroline and *i*-PrOH) purchased from Aldrich in the presence of catalyst **1** or **3**. [b] Isolated yield. [c] Conversion by GC analysis. [d] Triethylamine was added.

The catalytic activity of **3** in the reactions of 4-substituted-aryl Grignard reagents was also similar to that of **1**. The reactions of 4-tolyl-MgBr (**5b**) or 4-CF_3-C_6H_4-MgBr (**5c**) in the presence of 10 mol% of catalyst at 50 °C for 6 h gave homo-coupling products **6b** in 95% yield using **3** vs. 91% using **1** or **6c** in 92% using **3** vs. 91% using **1**, respectively. Although an advantageous use of **3** could not be found in the reaction of **5**, the superiority of **3** was shown in the homo-coupling of Grignard reagents

bearing thienyl groups (**7**) to give bithiophene derivatives **8**, which were utilized for the functional molecules.[9] The reaction of 2-thienyl magnesium bromide (**7a**) using 20 mol% of the oxidant **1** at 60 °C for 12 h gave only a low yield of 2,2'-bithiophene (**8a**) (Table 2, entry 2) unlike the reactions of **5**. In contrast, the reaction of **7a** using 20 mol% of **3** afforded 94% of **8a** (entry 1). In this case, 2(5*H*)-thiophenone as a by-product was observed in only ca. 2%. The organic catalyst **3** was effective for other Grignard reagents bearing thienyl group (**7b**-**7e**), and bithiophene products (**8b**-**8e**) were obtained in over 80% yields. On the contrary, the reactions using **1** produced the coupling products **8** in low yield. The results showed that the rate of electron-transfer from the Grignard reagent **7** with **1** was slower than that with **3**, and the active species **3** hardly formed from **1** during the reaction. When the reaction of 2-pyridyl-MgBr (**7f**) was performed using **3**, 2,2'-bipyridyl (**8f**) was obtained in 44% yield. However, the reaction of 2-furyl-MgBr did not proceed.

Table 2 Homo-coupling Reaction of Grignard Reagents bearing Thienyl Groups (**7**)[a]



entry	Grignard reagent	catalyst	time (h)	yield (%)[b]
1	 **7a**	**3**	12	94 (**8a**)
2		**1**	12	36 (**8a**)
3	 **7b**	**3**	24	88 (**8b**)
4		**1**	24	45 (**8b**)
5	 **7c**	**3**	24	82 (**8c**)
6		**1**	24	43 (**8c**)
7	 **7d**	**3**	24	85 (**8d**)
8		**1**	24	39 (**8d**)
9	 **7e**	**3**	24	80 (**8e**)
10		**1**	24	35 (**8e**)

[a] The use of 1.0 mmol of **7** (1.0 M THF solution, which was titrated with 1,10-phenanthroline and *i*-PrOH) in the presence of 20 mol% of **3** or **1**. [b] Isolated yield.

Finally, synthesis of (6,6'-dimethoxy[1,1'-biphenyl]-2,2'-diyl)bis-phosphonic acid tetraethyl ester (**9**) using catalyst **3** was demonstrated. The compound **9** has been used as a synthetic intermediate for the MeO-BIPHEP ligand and its derivatives.[10] Thus far, **9** had been synthesized using Ullman coupling of diethyl (2-iodo-3-methoxyphenyl)phosphonate[11] or oxidative coupling of lithium diethyl 3-methoxyphenylphosphonate.[12] Both the reactions mediated a stoichiometric transition metal (Cu[11] or $FeCl_3$[12]) to give **9** in medium yields (ca. 40%–60%). One of the great drawbacks of both reactions was the post-treatment of the reactions. After the coupling reactions, a tar-like paste of transition-metal origin obstructed the purification of **9**. The paste adhered to the surface of a filter, even if the Celite® was used, and filtration was made very difficult to be carried out, especially remarkable in large scale synthesis. Therefore, the synthesis of **9** using organocatalyst **3** was tried (Figure 3). The Grignard reagent was prepared from diethyl 3-methoxyphenylphosphonate (**10**) with LDA followed by the addition of $MgBr_2$ in THF. This was added to the THF solution containing 20 mol% of **3**, and the solution was then stirred at 60°C for 24 h to give the coupling product of **9** in 44% yield; at 48 h reaction time, the yield improved to 59%. Gram-scale synthesis was then tried

under the latter condition. In the scale of 2.9 g of **10**, a somewhat viscous and dark solution was obtained after the coupling reaction. The viscosity could be easily removed by filtration through a short pad of Celite®, and easy purification of the concentrated filtrate by silica-gel chromatography gave the 1.6 g of **9** in 55% yield.

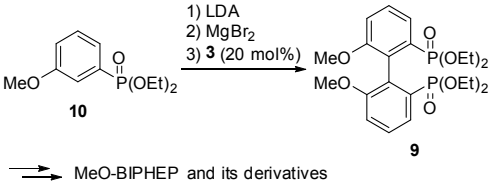


Figure 3 Synthesis of the synthetic intermediate of MeO-BIPHEP using **3**.

As a whole, in this and the authors' previous studies, oxidative coupling of RMgX using **3** or **1** gave homo-coupling products in high yield and high TON as compared to the reactions using the other two organocatalysts.[2a,2c, 2d] One of the reasons for this good result could be the inhibition of the formation of the by-product. For instance, the coupling reaction of PhMgBr using 20 mol% of TEMPO with continual bubbling of pure O_2 yields 61% and 24% biphenyl and a phenol, respectively.[2a] In contrast, the current study's catalytic reaction yielded only ca. 1% of phenol in entry 1 of Table 2. The explanation of the results is very difficult because the detail mechanism of the oxidative coupling of Grignard reagents is complicated and still unclear. One of the most feasible mechanism of the biaryl coupling is oxidant-mediated elimination of biaryl from Ar_2Mg,[13] and the aryl radical (Ar•) which was generated from ArMgBr with oxidant does not participate in the coupling. In contrast, the Ph• was observed in the reaction of PhMgBr using *p*-benzoquinone as an

oxidant in THF.[5d] Therefore, it can't be denied the possibility that Ar• is associated with the side reaction with O_2 to give oxidizing by-product such as phenol. As one possibility, the stabilization of Ph• with **2** was demonstrated by DFT calculations.–The interacted structure of Ph• with **2** was searched by DFT calculations at the uB97D/6-31+G(d) using Gaussian 09. As a result, the structure of {Ph• + **2** + $MgBr^+$[2 THF]} (**11**) was found (Figure 4). The two molecules of THF binding to Mg were very important for the stabilization of this structure (See Supporting Information). In the structure **11**, it was certain that Ph• and the anion species **2** existed (in other words, the phenyl anion and radical species **3** did not exist) because the sum of the Mulliken charges or the NPA charges of the phenyl ring were +0.07 or −0.06, and for the moiety of **2** ($C_{19}F_{17}$), they were −1.04 or −0.88 (Figure 5). Furthermore, the NPA charge (+0.10) and the natural electron configuration ($2s^{1.02}2p^{2.85}$) at the *ipso*-carbon of the phenyl ring in structure **11** were similar to those of the phenyl radical (+0.15; $2s^{1.02}2p^{2.82}$) but not those of the phenyl anion (−0.41; $2s^{1.23}2p^{3.13}$) (Figure S1 in Supporting Information). In the orbital analysis of the SOMO of **11**, the lobes were located at the *ipso*-carbon of the phenyl ring and the cyclopentadienyl ring (Figure 4). In contrast, the lobes at the *ipso*-carbon were not observed in SOMO-1 and SOMO-2 (See Supporting Information). The orbital distribution in the SOMO predicted the existence of an interaction between the *ipso*-carbon of phenyl ring and the cyclopentadienyl ring. NBO analysis clarified the relatively strong interaction of the natural bond orbital of the *ipso*-carbon [C^{ipso}(Lp)] with a localized anti-bonding orbital, C-C(π*) or C-C(σ*), in the cyclopentadienyl ring (Figure S2 in Supporting Information). The corresponding interacting

energies, computed using second-order perturbation theory [E(2)], were 11.96 or 12.12 kcal/mol, respectively. These relatively large interacting energies would play a role in the stabilization of Ph•. As a result, Ph• in **11** was stabilized by 11.6 kcal/mol as compared to free Ph• (Figure S3 in Supporting Information). Therefore, if Ph• was generated, the side reaction of Ph• to give phenol would be retarded.

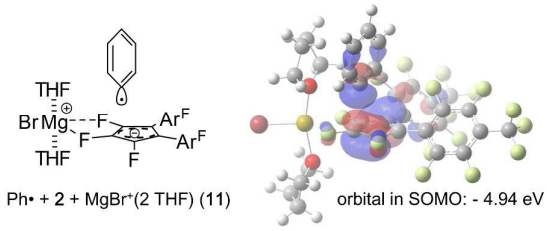


Figure 4 Optimized structure of **11**.

In summary, the radical species **3** could be alternative synthesized, and it acted as an organocatalyst for the oxidative homo-coupling of Grignard reagents. The catalyst showed a relatively high TON for the coupling of PhMgBr, and it enabled catalytic oxidative homo-coupling of Grignard reagents bearing thienyl groups to give bithiophene compounds. The catalytic system seemed to stabilize the radical intermediate derived from a Grignard reagent to inhibit the side reaction. In future work, it is expected that the radical species **3** will be diverted to the other oxidative reactions under aerobic condition.[14]

Experimental Section

General experimental methods.

All reactions were carried out under an argon atmosphere with dry solvents under anhydrous conditions, unless otherwise noted. All solvents were purchased from Kanto Chemical Co. and then were stored in Schlenk tubes under an argon atmosphere. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise noted. Preparative column chromatography was carried out by using silica gel (Kanto Chemical Co. 60N, 63-210 μm). ^{1}H NMR spectra were measured at 400 MHz or 500 MHz using tetramethylsilane (TMS) as an internal standard (δ 0 ppm). ^{13}C NMR spectra were measured at 101 MHz or 126 MHz, and chemical shifts are given relative to chloroform-*d* (δ 77.16 ppm). ^{19}F NMR spectra were measured at 376 MHz, and chemical shifts are given relative to CCl_3F using C_6F_6 as secondary reference (-162.9 ppm). ^{31}P NMR spectrum was measured at 162 MHz, and chemical shifts are given relative to 85% H_3PO_4 externally.

Formation of catalyst 3 from 1

A flame-dried 20 mL Schlenk flask was flushed with argon and charged with powder Magnesium (12.2 mg, 0.5 mmol), catalytic amount of I_2, 1,2-bisperfluorotolyl-3,3,4,4,5,5-hexafluorocyclopentene (**1**, 121.6 mg, 0.2 mmol) and THF (1.0 mL). The reaction mixture was stirred at 40 °C for 4 h under argon atmosphere to give dark brown solution. Then, the solution was expose to the dry air into the reactor. The reaction mixture was

turned to dark purple solution to form the radical active species **3**. The solution of **3** was used for the homo-coupling reactions without purification because the radical species **3** could not be isolated.

General Procedure for the Catalytic Homo-coupling Reaction of Grignard Reagent.

A 20 mL Schlenk flask was flushed with freshly prepared radical active species **3** (0.2 mmol, 20 mol%). And then, freshly prepared Grignard reagent in THF (1.0 mmol, titrated by using 1,10-phenanthroline and isopropanol) was added. The reaction mixture was stirred at appropriate temperature for 6 to 72 h under dry air. The reaction mixture was quenched with saturated aqueous NH_4Cl solution, and extracted with EtOAc or CH_2Cl_2. The organic layer was dried over Na_2SO_4 and was concentrated under reduced pressure. The resulting mixture was purified by silica gel column chromatography to give the corresponding product.

General Procedure for the Oxidative Homo-coupling Reaction of Grignard Reagent.

A flame-dried 20 mL Schlenk flask was flushed with argon and charged with 1,2-bisperfluorotolyl-3,3,4,4,5,5-hexafluorocyclopentene (**1**, 121.63 mg, 0.2 mmol) and THF (1.0 mL) at room temperature. And then, purchased or freshly prepared Grignard reagent in THF (1.0 mmol, titrated by using 1,10-phenanthroline and isopropanol) was added. The reaction mixture was stirred at appropriate temperature for 12 to 24 h under dry air. The reaction mixture was quenched with saturated aqueous NH_4Cl solution, and extracted with EtOAc or CH_2Cl_2. The organic layer was

dried over Na_2SO_4 and was concentrated under reduced pressure. The resulting mixture was purified by silica gel column chromatography to give the corresponding product.

Biphenyl (6a) [2b]

Catalytic homo-coupling of Ph-MgBr (**5a**, 1.0 mmol) was performed in the presence of 10 mol% **3** at 50 °C for 6 h to give **6a** (75.3 mg, 0.488 mmol, 98%) as a white solid. ^{1}H NMR (400 MHz, CDCl3): δ 7.30 - 7.36 (m, 2H), 7.40 - 7.45 (m, 4H), 7.57 - 7.60 (m, 4H). ^{13}C NMR (101 MHz, CDCl3): δ 127.3, 127.4, 128.9, 141.4.

4,4'-Dimethylbiphenyl (6b) [2b]

Catalytic homo-coupling of 4-tolyl-MgBr (**5b**, 1.0 mmol) was performed in the presence of 10 mol% **3** at 50 °C for 6 h to give **6b** (86.7 mg, 0.476 mmol, 95%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.39 (s, 6H), 7.24 (d, J = 8.0 Hz, 4H), 7.48 (d, J = 8.0 Hz, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.2, 126.9, 129.5, 136.8, 138.4.

4,4'-Bis(trifluoromethyl)biphenyl (6c) [2b]

Catalytic homo-coupling of 4-CF_3-C_6H_4-MgBr (**5c**, 1.0 mmol) was performed in the presence of 10 mol% **3** at 50 °C for 6 h to give **6c** (133.2 mg, 0.459 mmol, 92%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.72 (dd, J = 9.5, 8.5 Hz, 8H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 124.2 (q, J = 271.7

Hz), 126.0 – 126.1 (m), 127.7, 130.3 (q, J = 32.4 Hz), 143.3.

2,2'-Bithiophene (8a) [15]

Catalytic homo-coupling of 2-thienyl-MgBr (**7a**, 1.0 mmol) was performed in the presence of 20 mol% **3** at 60 °C for 12 h to give **8a** (78.2 mg, 0.470 mmol, 94%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.00 - 7.03 (m, 2H), 7.17 (d, J = 3.5 Hz, 2H), 7.20 (d, J = 5.1 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 123.9, 124.5, 127.9, 137.5

3,3'-Bithiophene (8b) [16]

Catalytic homo-coupling of 3-thienyl-MgBr (**7b**, 1.0 mmol) was performed in the presence of 20 mol% **3** at 60 °C for 24 h to give **8b** (73.0 mg, 0.439 mmol, 88%) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32 – 7.36 (m, 4H), 7.36 - 7.38 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 119.9, 126.2, 126.5, 137.3.

5,5'-Dimethyl-2,2'-bithiophene (8c) [17]

Catalytic homo-coupling of 5-Me-2-thienyl-MgBr (**7c**, 1.0 mmol) was performed in the presence of 20 mol% **3** at 60 °C for 24 h to give **8c** (79.8 mg, 0.411 mmol, 82%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.46 (s, 6H), 6.63 (d, J = 3.1 Hz, 2H), 6.87 (d, J = 3.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 15.5, 123.0, 125.9, 135.6, 138.6.

5,5'-Dimethyl-3,3'-bithiophene (8d) [18]

Catalytic homo-coupling of 5-Me-3-thienyl-MgBr (**7d**, 1.0 mmol) was performed in the presence of 20 mol% **3** at 60 °C for 24 h to give **8d** (82.8 mg, 0.426 mmol, 85%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (s, 6H), 6.95 (s, 2H), 7.05 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 15.5, 117.4, 124.7, 137.4, 140.3.

3,3'-Dimethyl-2,2'-bithiophene (8e) [19]

Catalytic homocoupling of 3-Me-2-thienyl-MgBr (**7e**, 1.0 mmol) was performed in the presence of 20 mol% **3** at 60 °C for 24 h to give **8e** (77.9 mg, 0.401 mmol, 80%) as a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.17 (s, 6H), 6.91 (d, J = 5.2 Hz, 2H), 7.25 (d, J = 5.2 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 14.8, 125.1, 129.5, 130.2, 136.6.

2,2'-Bipyridyl (8f) [20]

Catalytic homo-coupling of 2-pyridyl-MgBr (**7f**, 1.0 mmol) was performed in the presence of 20 mol% **3** at 60 °C for 24 h to give **8f** (34.5 mg, 0.221 mmol, 44%) as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 (t, J = 1.2 Hz, 2H), 7.82 (t, J = 1.2 Hz, 2H), 8.39 (d, J = 8.0 Hz, 2H), 8.68 (t, J = 2.0 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 121.2, 123.8, 137.0, 149.3, 156.2.

(6,6'-dimethoxy[1,1'-biphenyl]-2,2'-diyl)bis-phosphonic acid tetraethyl ester (9) [11]

Diisopropylamine (1.62 g, 16.0 mmol), 1.60 M *n*-BuLi (9.38 mL, 15.0 mmol), THF (10 mL) were added to the flame-dried 50 mL Schlenk flask **A** under argon. The reaction mixture was stirred at -78 °C for 30 min. After addition of a solution of diethyl-3-methoxyphenylphosphonate (**10**) (3.42 g, 14.0 mmol) in 5 mL of THF to the solution dropwise, the reaction mixture was stirred at -78 °C for 1 h.

To another flame-dried 50 mL Schlenk flask **B** flushed with argon, magnesium powder (390 mg, 16.0 mmol) and THF (10 mL) was added at 0 °C. After addition of 1,2-dibromoethane (2.82 g, 15.0 mmol) to the solution dropwise, the turbid solution was stirred at 0 °C to room temperature for 2 h. The resulting solution was slowly added to the Schlenk **A**, and the reaction mixture was stirred for 1 h at room temperature to give the corresponding Grignard reagent.

The prepared Grignard reagent (12.0 mmol, titrated by using 1,10-phenanthroline and isopropanol) was added to the THF solution of **3** (from 1.46 g of **1**, 2.4 mmol, 20 mol%) in 50 mL Schlenk flask. The reaction mixture was stirred at 60 °C for 48 h under dry air. The reaction mixture was quenched with saturated aqueous NH_4Cl solution, and extracted with EtOAc. The organic layer was dried over Na_2SO_4 and was concentrated under reduced pressure. The resulting mixture was purified by silica gel column chromatography to give **9** (1.60 g, 3.29 mmol, 55%) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.12 (t, J = 7.1 Hz, 6H), 1.16 (t, J = 7.1 Hz, 6H), 3.71 (s, 6H), 3.76 – 3.94 (m, 8H), 7.11 (d, J = 8.2 Hz, 2H), 7.42 (m, 2H), 7.56 (m, 2H). ^{31}P NMR (162 MHz, $CDCl_3$): δ 18.0 (s).

^{13}C NMR (101 MHz, $CDCl_3$): δ 16.3 (t, J = 6.9 Hz), 55.9, 61.5 (d, J = 5.7 Hz), 61.6 (d, J = 6.1 Hz), 125.0 (d, J = 8.6 Hz), 128.4, 128.6, 129.1, 129.5 – 129.8 (m), 131.0, 157.6 (d, 19.8 Hz).

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Supporting Information

The copies of NMR spectra and computational data. This material is available free of charge via the Internet at http://pubs.acs.org.

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6 Purification of **1** was required before performing the conversion of **1** to the active species **3**, if **1** was stored in the atmosphere. Although no appreciable change of **1** was observed after storing under argon for a month by ^{19}F NMR and GC-MS analyses, **1** was allowed to stand under argon with moisture for a month to give ca. 10% of decomposed impurity. The impurity could be removed by silica-gel column chromatography and recrystallization.

7 In the ESR spectrum, a broad singlet peak at the position of g = 2.00268 was observed at room temperature, which is the evidence of the presence of a radical in the THF solution. The radical can be expected to be the cyclopentadienyl radical **3** generated by one-electron oxidation of the cyclopentadienyl anion **2**, considering the g-value is in good agreement with that of **3** generated in the homo-coupling reaction (g = 2.00309). See ref. 2b.

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