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# Direct coupling of arenes and iodoarenes catalyzed by a rhodium complex with a strongly π-accepting phosphite ligand

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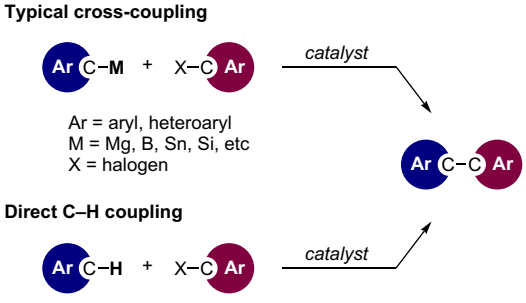
**Abstract**

A new rhodium-based catalytic system for the direct C–H coupling of arenes and iodoarenes that shows high activity with reasonably broad scope was developed. Under the catalytic influence of $RhCl(CO)\{P[OCH(CF_3)_2]_3\}_2$ and $Ag_2CO_3$, the direct C–H arylation of heteroarenes and arenes took place with iodoarenes to afford a range of biaryls in good to excellent yields with high regioselectivity. Thiophenes, furans, pyrroles, indoles, and alkoxybenzenes are applicable to this arylation protocol.


## 1. Introduction

Organic molecules having (hetero)aryl–(hetero)aryl bonds represent privileged structural motifs frequently found in natural products or used in pharmaceuticals and functional organic materials. Therefore, the development of efficient methods for biaryl formation has been a topic of great importance in all aspects of pure and applied chemistry.[1] Currently, the palladium-catalyzed cross-coupling reactions of metalated arenes and halogenated arenes (Ar–M+Ar–X→Ar–Ar+M–X) are undoubtedly among the most important and reliable methodologies for making biaryls (Scheme 1).[1,2] The development of improved catalysts and reagents continues to evolve at a rapid pace, and many important organic substances (pharmaceuticals as well as advanced electronic and photonic materials) are now made using this technology.[2] However, there is a common limitation and inefficiency in this cross-coupling technology: it requires extra steps to install the metallic fragments on arenes.




Scheme 1. Synthesis of biaryls through typical cross-coupling and direct C–H coupling catalyzed by transition metal complexes.

By contrast, the direct C–H coupling of arenes and haloarenes (Ar–H+Ar–X→Ar–Ar+H–X) offers the promise of a solution to many of these drawbacks and therefore holds significant synthetic potential (Scheme 1).[3,4] Indeed, recent worldwide research has resulted in impressive progress for the direct C–H coupling methodology in making biaryls (mainly palladium-based systems).[3–11] However, there still exists considerable room for further development. For example, a universal catalyst that can directly arylate all heteroarenes as well as simple arenes has not been forthcoming (Scheme 1).

As a part of our program aimed at establishing programmed synthesis of (hetero)arene-core functional molecules,[12] we recently reported that a direct coupling of arenes and iodoarenes proceeds with the agency of a catalytic amount of $RhCl(CO)\{P[OCH(CF_3)_2]_3\}_2$ (**1**) and silver carbonate, furnishing

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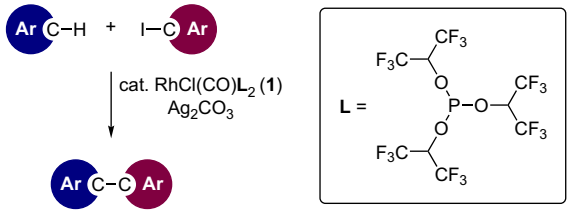
privileged biaryls in good to excellent yields (Scheme 2).[13] Herein we report the details of this study in full.

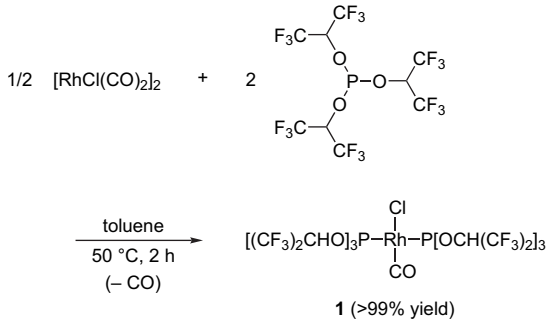



Scheme 2. Direct coupling of arenes and iodoarenes catalyzed by Rh/$P[OCH(CF_3)_2]_3$/$Ag_2CO_3$ system.

## 2. Results and discussion

### 2.1. Synthesis and structure of rhodium complex *1*

The synthesis of $RhCl(CO)\{P[OCH(CF_3)_2]_3\}_2$ (**1**) is straightforward and easy to conduct (Scheme 3). Thus, a solution of $[RhCl(CO)_2]_2$ and $P[OCH(CF_3)_2]_3$ in dry toluene was stirred at 50 °C for 2 h under argon. After cooling the reaction mixture to room temperature, solvent was removed under reduced pressure. Reprecipitation from THF/toluene followed by filtration and vacuum drying afforded **1** as yellow solid (>99% yield). This complex is very stable in air and moisture in the solid state. Virtually no decomposition of **1** has been detected after extended (>10 months) exposure to air.




Scheme 3. Synthesis of rhodium complex **1**.

The X-ray crystal structure of **1** indicates that the high stability of **1** may be due to the effective shielding of the rhodium atom by two bulky phosphite ligands (Fig. 1). In addition, a 'push' electronic effect of Cl, rendering the rhodium center less unsaturated than a formal 16-electron species through a π-donation from Cl to Rh, might also contribute to its high stability.[14,15]

### 2.2. Discovery of rhodium catalysis

We discovered that the rhodium complex **1** functions as an efficient catalyst precursor, with the assistance of silver carbonate, for the direct coupling of electron-rich heteroarenes and iodoarenes. For example, when a mixture of 3-methoxythiophene (**2a**) and iodobenzene (**3a**) in *m*-xylene was stirred at 150 °C for 12 h in the presence of **1**, $Ag_2CO_3$, and 1,2-dimethoxyethane

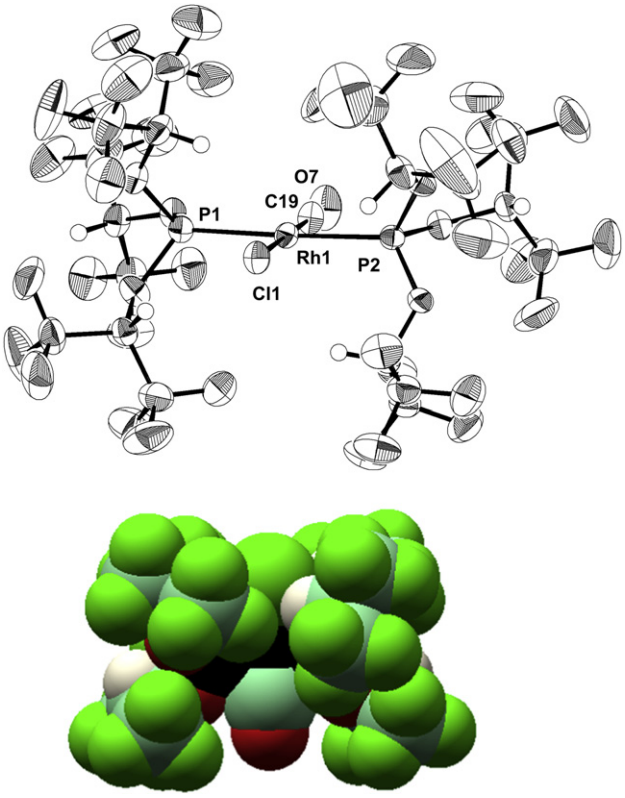
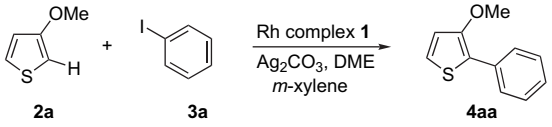



Figure 1. The X-ray structure of **1** (upper: ORTEP drawing, bottom: space-filling model). Thermal ellipsoids are drawn at the 50% probability level.

(DME) (**1**/**2a**/**3a**/$Ag_2CO_3$/DME=0.03:1.5:1.0:1.0:1.0 molar ratio), a direct C–H coupling took place at the 2-position of **2a** to afford **4aa** in 75% yield with virtually complete regioselectivity (Scheme 4).[16] When the reaction was conducted at 200 °C under microwave irradiation, the reaction was complete within 0.5 h to furnish **4aa** in 73% yield.




**1**/**2a**/**3a**/$Ag_2CO_3$/DME = 0.03:1.5:1.0:1.0:1.0 mol ratio

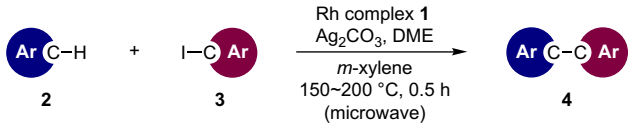
*75% (150 °C, 12 h)*
*73% (200 °C, 0.5 h, μW)*

Scheme 4. Direct coupling of 3-methoxythiophene and iodobenzene catalyzed by Rh/$P[OCH(CF_3)_2]_3$/$Ag_2CO_3$ system.

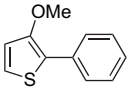
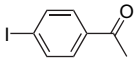
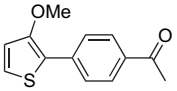
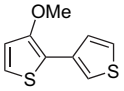
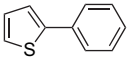
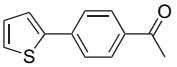
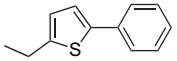
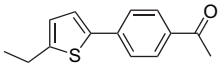
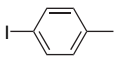
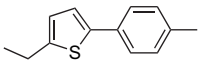
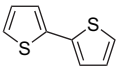
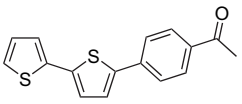
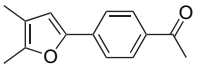
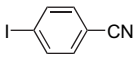
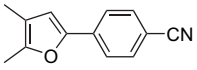
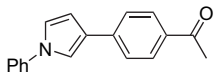
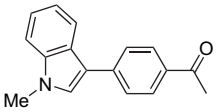
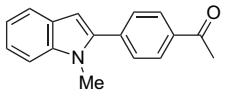
### 2.3. Direct coupling of heteroarenes and iodoarenes

With a new rhodium-based system catalyzing the direct C–H coupling in hand, we surveyed heteroarenes and haloarenes that could be applied to our system (Table 1). We first identified that the direct coupling proceeded efficiently with electron-neutral and electron-deficient iodoarenes by using **2a** as a model substrate. Electron-rich iodoarenes and iodoheteroarenes were also found to be applicable, but they tend to possess somewhat lower reactivity. Unfortunately, the corresponding bromides, chlorides, and triflates were found to be poor substrates with this first-generation catalytic system.

Table 1
Direct coupling of heteroarenes and iodoarenes catalyzed by **1**[a]




**2** **3** **4**

| Entry | 2 | 3 | Product 4 | Yield[b] (%) |
|---|---|---|---|---|
| 1 |  **2a** |  **3a** |  **4aa** | 73 (80) |
| 2 | **2a** |  **3b** |  **4ab** | 94 (99) |
| 3 | **2a** |  **3c** |  **4ac** | 52 (58) |
| 4 |  **2b** | **3a** |  **4ba** | 53 (80)[c] |
| 5 | **2b** | **3b** |  **4bb** | 83[c] |
| 6 |  **2c** | **3a** |  **4ca** | 76 (99) |
| 7 | **2c** | **3b** |  **4cb** | 79 (87) |
| 8 | **2c** |  **3d** |  **4cd** | 50 (64) |
| 9 |  **2d** | **3b** |  **4db** | 64 |
| 10 |  **2e** | **3b** |  **4eb** | 64 |
| 11 | **2e** |  **3e** |  **4ee** | 66 |
| 12 |  **2f** | **3b** |  **4fb** | 58 (86) |
| 13 |  **2g** | **3b** |  **4gb** (C-3) | 57 |
| | | |  **4gb'** (C-2) | 23 |

[a] Molar ratio: **1/2/3**/$Ag_2CO_3$/DME=0.03:1.5:1.0:1.0:1.0.
[b] Isolated yield. The yield in parentheses is determined by NMR.
[c] Molar ratio: **1/2/3**/$Ag_2CO_3$/DME=0.1:15:1.0:1.0:0. Reactions were conducted under conventional heating (150 °C, 14–15 h).

As for heteroarenes, we found that a range of electron-rich five-membered heteroarenes, such as thiophenes, furans, pyrroles, and indoles, were applicable to the present catalysis (Table 1). Not only 3-methoxythiophene (**2a**), but also thiophene (**2b**), 2-ethylthiophene (**2c**), and bithiophene (**2d**) were found to cross-couple with iodoarenes, affording the corresponding biaryls in good yields (entries 1–9). Furans such as 2,3-dimethylfuran (**2e**) were also arylated well (entries 10 and 11). For all thiophenes and furans examined, the direct coupling proceeded selectively at carbons adjacent to sulfurs or oxygens. When 1-phenylpyrrole (**2f**) was used as a substrate, the direct coupling with **3b** took place selectively at the 3-position of the pyrrole ring (entry 12). The direct coupling of 1-methylindole (**2g**) and **3b** also took place efficiently, but resulted in a 71:29 mixture of regioisomers favoring the C3-arylation product (entry 13). Unfortunately, the C–H coupling did not proceed with electron-deficient six-membered heteroarenes such as pyridine using our first-generation catalyst.

### 2.4. Mechanistic considerations

Although the precise mechanism remains unknown, our current approximation is shown in Figure 2. We surmise that ligand dissociation (most likely the phosphite) from **1** is an initial step generating a coordinatively unsaturated rhodium(I) species **A**, which thereafter initiates a $Rh^{I}/Rh^{III}$ redox cycle.[13] This includes (i) oxidative addition of iodoarene **3** (Ar–I) to **A**, (ii) generation of cationic arylrhodium(III) species **B** with the assistance of silver carbonate, (iii) electrophilic metalation (rhodation) of arene **2** (Ar–H) with **B** giving diarylrhodium(III) species **C**, and (iv) reductive elimination of biaryl product (**4**) with the regeneration of **A**.[17,18]

The beneficial effect of strongly π-accepting $P[OCH(CF_3)_2]_3$ might be to render the rhodium center electron-deficient, thereby facilitating electrophilic metalation as well as a reductive elimination step. A preliminary experimental study using deuterium-labeled substrates is in line with such an assumption. For example, when deuterium-labeled thiophene was subjected to the coupling with iodobenzene under the influence of **1** and $Ag_2CO_3$, both C–H and C–D bonds adjacent to sulfur were phenylated to a degree virtually equal, indicating a negligible kinetic isotope effect (Scheme 5). This result indicates that the C–H bond-cleaving step (possibly electrophilic rhodation; **B**→**C** in Fig. 2) is not a turnover-limiting step in our catalysis.

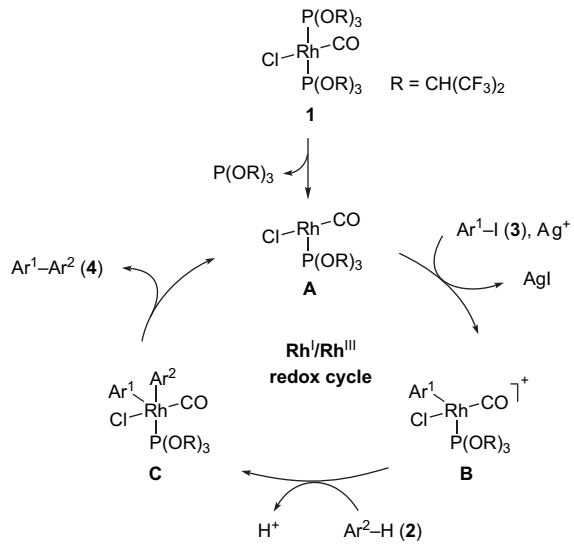
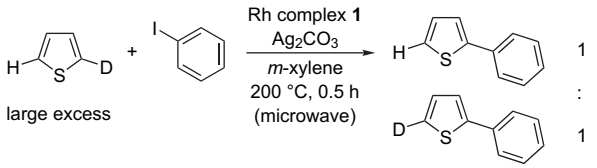


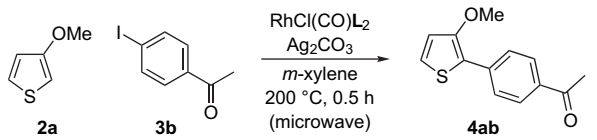

Figure 2. A possible mechanism of our rhodium catalysis.




Scheme 5. Intramolecular competitive reaction using deuterium-labeled thiophene.

In line with our mechanistic assumption that the use of strongly π-accepting $P[OCH(CF_3)_2]_3$ as a ligand has a strong impact on the energetic profile in the catalytic cycle, we observed a strong ligand effect in the present catalysis (Table 2). For example, when a less π-accepting ligand such as $P(C_6H_5)[OCH(CF_3)_2]_2$, $P(OC_6H_5)_3$, $P[OCH(CH_3)_2]_3$, and $P(C_6H_5)_3$ was used in place of $P[OCH(CF_3)_2]_3$ for the reaction of **2a** and **3b**, the yield of the arylation product **4ab** decreased from 94% to 31%, 6%, 9%, and 0%, respectively (Table 2). There is a clear correlation between the arylation efficiency and the π-accepting ability of the ligand, as judged by electronic parameters[19] based on the carbonyl stretching frequency ($\nu_{CO}$) in *trans*-RhCl(CO)$\mathbf{L}_2$ complexes. In particular, the dramatic difference between $P[OCH(CF_3)_2]_3$ and $P[OCH(CH_3)_2]_3$, which are almost identical in size, is a clear indication that the π-accepting nature of the ancillary ligand has the greatest benefit in our catalysis.

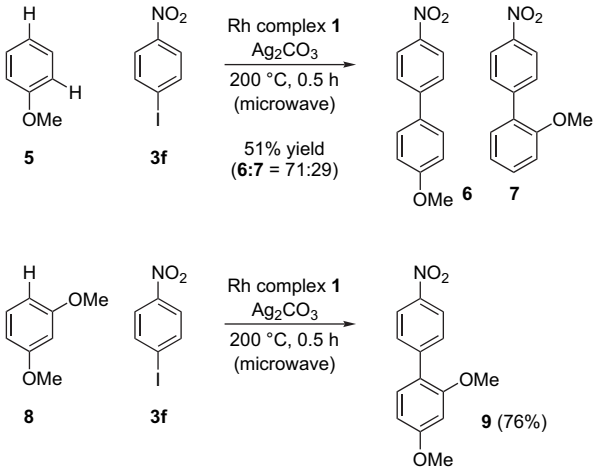
Table 2
Effect of ligand in Rh-catalyzed direct coupling




| Ligand (**L**) | Yield of **4ab** (%) | $\nu_{CO}$ in RhCl(CO)$\mathbf{L}_2$ ($cm^{-1}$) |
|---|---|---|
| **$P[OCH(CF_3)_2]_3$** | **94** | **2070** |
| $P(C_6H_5)[OCH(CF_3)_2]_2$ | 31 | 2038 |
| $P(OC_6H_5)_3$ | 6 | 2018 |
| $P[OCH(CH_3)_2]_3$ | 9 | 2002 |
| $P(C_6H_5)_3$ | 0 | 1983 |

### 2.5. Direct coupling of benzene derivatives and iodoarenes

The aforementioned substrate survey (Table 1) revealed that our first-generation catalyst has a reasonably broad scope of substrates but is not yet truly universal, which encourages us to develop it further. However, we found that our catalyst can

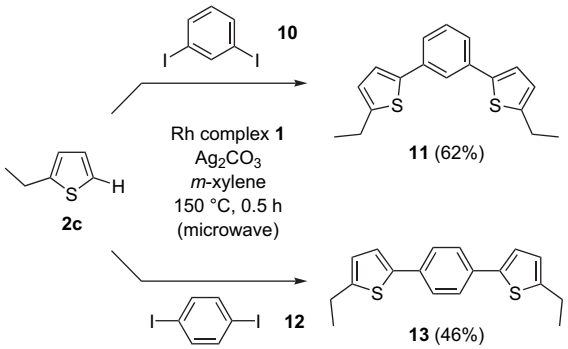



Scheme 6. Arylation of benzene derivatives.

effect the direct C–H coupling of benzene derivatives, which have proven to be the most challenging substrate class in this field (Scheme 6).[3,4] For example, when anisole (**5**) was treated with *p*-nitrophenyl iodide (**3f**) under the influence of **1** and $Ag_2CO_3$ (**1/3f/5**/$Ag_2CO_3$=0.05:1.0:27:1.0 molar ratio), arylated anisoles (**6** and **7**) were obtained as a mixture of regioisomers (51% yield; *o*/*m*/*p*=29:0:71).[20] When 1,3-dimethoxybenzene (**8**) was used as a substrate, arylation occurred exclusively at the 4-position giving the corresponding biaryl **9** in 76% yield. These reactions not only serve as successful examples of the functionalization of relatively simple benzene derivatives, but also shed some light on the mechanism. The manifestation of clear *ortho–para* selectivity in the arylation of alkoxybenzenes is consistent with the C–H bond cleavage based on electrophilic metalation (Fig. 2) but not with those through directed *ortho*-metalation and/or C–H oxidative addition as have been proposed in some other C–H bond functionalization reactions.[4] A preliminary examination revealed that C–H arylation of alkylbenzenes also took place, albeit with low efficiency. Nevertheless, the successful arylation of benzene derivatives without catalyst-directing groups is noteworthy.[4]

### 2.6. Synthesis of extended π-systems through multiple C–H coupling

We envisage that the current direct C–H coupling technology has broad potential for further applications. For example, a range of extended π-electron systems can be easily constructed through multiple C–H coupling. When 1,3-diiodobenzene (**10**) was treated with an excess amount of 2-ethylthiophene (**2c**, 5.0 equiv to **10**), a double C–H arylation took place giving an interesting benzene-core π-system **11** in 62% yield (Scheme 7). When 1,4-diiodobenzene (**12**) was used as a core substrate, fully conjugated π-system **13** was obtained in 46% yield (Scheme 7). On the basis of these preliminary but promising results, we are currently working on the generation of novel functional oligoarenes using our direct C–H coupling technology.




Scheme 7. Synthesis of benzene-core π-systems (**11** and **13**) through multiple C–H coupling.

## 3. Conclusion

In summary, a new rhodium-based catalytic system for the direct C–H coupling of electron-rich arenes and iodoarenes that shows high activity with reasonably broad scope was developed. In many aspects, the present reaction can be best described as a Friedel–Crafts-type arylation of arenes. Elucidation of the reaction mechanism, development of second-generation catalysts, and applications of the direct arylation technology to materials science and pharmaceutical chemistry are currently underway.

## 4. Experimental

### 4.1. General

Unless otherwise noted, all materials including dry solvents (toluene and *m*-xylene) were obtained from commercial suppliers and used without further purification. The ligand $P[OCH(CF_3)_2]_3$ was prepared according to procedures reported in the literature.[21] Unless otherwise noted, all reactions were performed with dry solvents under an atmosphere of argon in flame-dried glassware with standard vacuum-line techniques. All coupling reactions using conventional heating were carried out in glass vessels equipped with J. Young® O-ring tap, heated in a 8-well reaction block (heater+magnetic stirrer). All microwave reactions were performed in a regularly calibrated CEM Focused Microwave™ Synthesis System (Discover) with IR temperature monitor and non-invasive pressure transducer using 10 mL vials with septa. All work-up and purification procedures were carried out with reagent-grade solvents in air. Preparative recycling gel permeation chromatography (GPC) was performed with a JAI LC-9204 instrument equipped with JAIGEL-1H/JAIGEL-2H columns using chloroform as an eluent. High-resolution mass spectra (HRMS) were obtained from a Waters Micromass LCT Premier (electrospray ionization time-of-flight mass spectrometry, ESI-TOFMS) or a JEOL JMS-700 (fast atom bombardment mass spectrometry, FABMS). Infrared spectra were recorded on a JASCO FTIR-6100 spectrometer. Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL JNM-ECA-600 ($^1$H 600 MHz, $^{13}$C 150 MHz, $^{31}$P 243 MHz) spectrometer. Chemical shifts for $^1$H NMR are expressed in parts per million (ppm) relative to

tetramethylsilane ($\delta$ 0.0 ppm). Chemical shifts for $^{13}C$ NMR are expressed in parts parts per million relative to $CDCl_3$ ($\delta$ 77.0 ppm). Chemical shifts for $^{31}P\{^1H\}$ NMR are reported downfield in parts per million relative to external 85% $H_3PO_4$ ($\delta$ 0.0 ppm). Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, dd=doublet of doublets, t=triplet, q=quartet, m=multiplet, br=broad signal), coupling constant (Hz), and integration. The structures of arylation products were determined based on 2D NMR experiments.

### 4.2. Synthesis and crystal structure analysis of rhodium complex *1*

A solution of $[RhCl(CO)_2]_2$ (200.4 mg, 0.51 mmol) and $P[OCH(CF_3)_2]_3$ (1.09 g, 2.06 mmol) in dry toluene (2.0 mL) was stirred at 50 °C for 2 h under argon. After cooling the reaction mixture to room temperature, solvent was removed under reduced pressure. Reprecipitation from THF/toluene followed by filtration and vacuum drying afforded *trans*-RhCl(CO)-$\{P[OCH(CF_3)_2]_3\}_2$ (**1**: 1.25 g, quant) as yellow solid. $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 5.64 (br, 6H). $^{31}P\{^1H\}$ NMR (243 MHz, THF-$d_8$) $\delta$ 123.3 (d, $J_{Rh-P}$=224 Hz). IR (KBr) 2070, 1371, 1302, 1250, 1207, 1113, 1088 $cm^{-1}$. Single crystals suitable for X-ray analysis were obtained by slow diffusion of toluene into an acetonitrile solution of **1**. Intensity data were collected at 173 K on a Rigaku Single Crystal CCD X-ray Diffractometer (Saturn 70 with MicroMax-007) with graphite-monochromated Mo K$\alpha$ radiation. A total of 30,758 reflections were corrected, of which 8832 were independent reflections ($R_{int}$=0.0312). The structure was solved by direct methods (SHELXS-97[22]) and refined by the full-matrix least-squares on $F^2$ (SHELEXL-97[22]). All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined isotropically. The crystal data are as follows: $C_{19}H_6ClF_{36}O_7P_2Rh$, $FW$=1230.54, crystal size 0.20×0.20×0.20 $mm^3$, monoclinic, space group $C2/c$ (No. 15). $a$=33.050(5) Å, $b$=17.903(2) Å, $c$=13.525(2) Å, $\alpha$=90.0000(5)°, $\beta$=105.3324(7)°, $\gamma$=90.0000(5)°, $V$=7717.8(19) $Å^3$, $Z$=4, $D_c$=1.059 g/$cm^3$. The refinement converged to $R_1$=0.0419, $wR_2$=0.1010 ($I>2s(I)$), GOF=1.105. Selective bond length (Å): Rh(1)–Cl(1)=2.3561(8), Rh(1)–P(1)=2.2597(8), Rh(1)–P(2)=2.2550(7), Rh(1)–C(19)=1.853(3), C(19)–O(7)=1.127(4). Selected angles (°): P(1)–Rh(1)–Cl(1)=90.90(3), Cl(1)–Rh(1)–P(2)=89.87(3), P(2)–Rh(1)–C(19)=89.74(9), C(19)–Rh(1)–P(1)=89.50(9), P(1)–Rh(1)–P(2)=177.93(3), Cl(1)–Rh(1)–C(19)=179.58(10), Rh(1)–C(19)–O(7)=179.5(3).

### 4.3. Typical procedure for coupling of heteroarenes and iodoarenes (conventional heating protocol)

#### 4.3.1. 3-Methoxy-2-phenylthiophene (*4aa*)

A 20-mL glass vessel equipped with J. Young® O-ring tap, containing a magnetic stirring bar, was flame-dried under vacuum and filled with argon after cooling to room temperature. To this vessel were added Rh complex **1** (14.9 mg, 12 μmol), $Ag_2CO_3$ (111.9 mg, 0.41 mmol), 1,2-dimethoxyethane (36.0 mg, 0.40 mmol), 3-methoxythiophene (**2a**: 68.5 mg, 0.60 mmol), iodobenzene (**3a**: 81.6 mg, 0.40 mmol), and dry *m*-xylene (2.0 mL) under a stream of argon. The vessel was sealed with O-ring tap, and then heated at 150 °C for 12 h in a 8-well reaction block with stirring. After cooling the reaction mixture to room temperature, the mixture was passed through a short silica gel pad (EtOAc/$CHCl_3$). The filtrate was evaporated and the residue was subjected to gel permeation chromatography ($CHCl_3$) to afford 3-methoxy-2-phenylthiophene (**4aa**: 57.1 mg, 75%) as pale yellow oil. $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 3.91 (s, 3H), 6.92 (d, $J$=5.5 Hz, 1H), 7.14 (d, $J$=5.5 Hz, 1H), 7.21 (t, $J$=7.6 Hz, 1H), 7.35 (t, $J$=7.6 Hz, 2H), 7.73 (d, $J$=7.6 Hz, 2H). $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 58.7, 117.5, 120.2, 122.1, 126.4, 126.9, 128.5, 133.4, 153.7. HRMS (ESI-TOF) $m/z$ calcd for $C_{11}H_{11}OS$ $[MH]^+$: 191.0531, found: 191.0540.

### 4.4. Typical procedure for coupling of heteroarenes and iodoarenes (microwave heating protocol)

A 10-mL flame-dried microwave vial containing a magnetic stirring bar was fitted with a septum and cooled under a stream of argon. To this vial were added Rh complex **1** (18.8 mg, 15 μmol), $Ag_2CO_3$ (138.7 mg, 0.50 mmol), 1,2-dimethoxyethane (45.1 mg, 0.50 mmol), 3-methoxythiophene (**2a**: 86.6 mg, 0.75 mmol), iodobenzene (**3a**: 102.0 mg, 0.50 mmol), and dry *m*-xylene (2.5 mL). The vial was sealed and heated with stirring at 200 °C for 30 min in a CEM Discover microwave apparatus. After the reaction vial was cooled down to room temperature, the mixture was passed through a short silica gel pad (EtOAc/$CHCl_3$). The filtrate was evaporated and the residue was subjected to gel permeation chromatography ($CHCl_3$) to afford **4aa** (69.7 mg, 73%) as pale yellow oil.

#### 4.4.1. 2-(p-Acetylphenyl)-3-methoxythiophene (*4ab*)

Isolated yield, 94% (99% NMR yield) from 3-methoxythiophene (**2a**) and 4-iodoacetophenone (**3b**) (microwave heating, 200 °C, 30 min). $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 2.59 (s, 3H), 3.95 (s, 3H), 6.94 (d, $J$=5.5 Hz, 1H), 7.24 (d, $J$=5.5 Hz, 1H), 7.83 (d, $J$=8.9 Hz, 2H), 7.94 (d, $J$=8.9 Hz, 2H). $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 26.5, 58.7, 117.3, 118.7, 124.0, 126.2, 128.7, 134.4, 138.3, 155.3, 197.4. HRMS (ESI-TOF) $m/z$ calcd for $C_{13}H_{13}O_2S$ $[MH]^+$: 233.0636, found: 233.0635.

#### 4.4.2. 3-Methoxy-2,3′-bithiophene (*4ac*)

Isolated yield, 52% (58% NMR yield) from 3-methoxythiophene (**2a**) and 3-iodothiophene (**3c**) (microwave heating, 200 °C, 30 min). $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 3.92 (s, 3H), 6.88 (d, $J$=5.5 Hz, 1H), 7.06 (d, $J$=5.5 Hz, 1H), 7.29 (dd, $J$=4.8, 2.8 Hz, 1H), 7.38 (dd, $J$=4.8, 1.4 Hz, 1H), 7.57 (dd, $J$=2.8, 1.4 Hz, 1H). $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 58.6, 116.0, 116.9, 119.5, 121.1, 125.2, 126.5, 133.3, 153.4. HRMS (ESI-TOF) $m/z$ calcd for $C_9H_9OS_2$ $[MH]^+$: 197.0095, found: 197.0094.

#### 4.4.3. 2-Phenylthiophene (*4ba*)[23]

Isolated yield, 53% (80% NMR yield) from thiophene (**2b**) and iodobenzene (**3a**) (conventional heating, 150 °C, 15 h).

Molar ratio: **1/2b/3a**/$Ag_2CO_3$/DME=0.1:15:1.0:1.0:0. $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 7.08 (dd, $J$=5.5, 3.4 Hz, 1H), 7.26–7.29 (m, 2H), 7.31 (d, $J$=3.4 Hz, 1H), 7.38 (t, $J$=8.2 Hz, 2H), 7.62 (d, $J$=8.2 Hz, 2H). $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 123.1, 124.8, 126.0, 127.4, 128.0, 128.9, 134.4, 144.4.

*4.4.4. 2-(p-Acetylphenyl)thiophene (**4bb**)*[24]

Isolated yield, 83% from thiophene (**2b**) and 4-iodoacetophenone (**3b**) (conventional heating, 150 °C, 14 h). Molar ratio: **1/2b/3b**/$Ag_2CO_3$/DME=0.1:15:1.0:1.0:0. $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 2.61 (s, 3H), 7.12 (dd, $J$=4.8, 3.4 Hz, 1H), 7.37 (dm, $J$=4.8 Hz, 1H), 7.43 (d, $J$=3.4 Hz, 1H), 7.69 (d, $J$=7.6 Hz, 2H), 7.96 (d, $J$=7.6 Hz, 2H). $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 26.5, 124.6, 125.6, 126.4, 128.3, 129.1, 135.8, 138.8, 142.9, 197.2.

*4.4.5. 2-Ethyl-5-phenylthiophene (**4ca**)*

Isolated yield, 76% (99% NMR yield) from 2-ethylthiophene (**2c**) and iodobenzene (**3a**) (microwave heating, 200 °C, 30 min). $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 1.34 (t, $J$=7.6 Hz, 3H), 2.86 (q, $J$=7.6 Hz, 2H), 6.75 (d, $J$=3.4 Hz, 1H), 7.12 (d, $J$=3.4 Hz, 1H), 7.23 (t, $J$=7.6 Hz, 1H), 7.34 (t, $J$=7.6 Hz, 2H), 7.56 (d, $J$=7.6 Hz, 2H). $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 15.9, 23.6, 122.7, 124.3, 125.5, 127.0, 128.8, 134.8, 141.6, 147.2. HRMS (FAB) *m/z* calcd for $C_{12}H_{12}S$ $[M]^+$: 188.0660, found: 188.0661.

*4.4.6. 2-(p-Acetylphenyl)-5-ethylthiophene (**4cb**)*

Isolated yield, 79% (87% NMR yield) from 2-ethylthiophene (**2c**) and 4-iodoacetophenone (**3b**) (microwave heating, 200 °C, 30 min). $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 1.34 (t, $J$=7.6 Hz, 3H), 2.58 (s, 3H), 2.87 (q, $J$=7.6 Hz, 2H), 6.78 (d, $J$=3.4 Hz, 1H), 7.23 (d, $J$=3.4 Hz, 1H), 7.61 (d, $J$=8.3 Hz, 2H), 7.92 (d, $J$=8.3 Hz, 2H). $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 15.7, 23.6, 26.5, 124.4, 124.8, 125.0, 129.0, 135.2, 139.1, 140.0, 149.2, 197.2. HRMS (ESI-TOF) *m/z* calcd for $C_{14}H_{15}OS$ $[MH]^+$: 231.0844, found: 231.0843.

*4.4.7. 2-Ethyl-5-p-tolylthiophene (**4cd**)*

Isolated yield, 50% (64% NMR yield) from 2-ethylthiophene (**2c**) and 4-iodotoluene (**3d**) (microwave heating, 180 °C, 30 min). $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 1.33 (t, $J$=7.6 Hz, 3H), 2.34 (s, 3H), 2.85 (q, $J$=7.6 Hz, 2H), 6.73 (d, $J$=3.4 Hz, 1H), 7.07 (d, $J$=3.4 Hz, 1H), 7.15 (d, $J$=7.6 Hz, 2H), 7.44 (d, $J$=7.6 Hz, 2H). $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 15.9, 21.1, 23.6, 122.1, 124.2, 125.4, 129.4, 132.0, 136.8, 141.7, 146.6. HRMS (FAB) *m/z* calcd for $C_{13}H_{14}S$ $[M]^+$: 202.0816, found: 202.0819.

*4.4.8. 5-(p-Acetylphenyl)-2,2′-bithiophene (**4db**)*

Isolated yield, 64% from 2,2′-bithiophene (**2d**) and 4-iodoacetophenone (**3b**) (microwave heating, 200 °C, 30 min). $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 2.61 (s, 3H), 7.04 (dd, $J$=5.5, 4.1 Hz, 1H), 7.17 (d, $J$=3.4 Hz, 1H), 7.23 (d, $J$=3.4 Hz, 1H), 7.25 (d, $J$=5.5 Hz, 1H), 7.34 (d, $J$=4.1 Hz, 1H), 7.67 (d, $J$=8.3 Hz, 2H), 7.96 (d, $J$=8.3 Hz, 2H). $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 26.5, 124.1, 124.8, 124.9, 125.27, 125.33, 128.0, 129.1, 135.7, 137.0, 138.4, 138.5, 141.4, 197.2. HRMS (ESI-TOF) *m/z* calcd for $C_{16}H_{13}OS_2$ $[MH]^+$: 285.0408, found: 285.0416.

*4.4.9. 2-(p-Acetylphenyl)-4,5-dimethylfuran (**4eb**)*

Isolated yield, 64% from 2,3-dimethylfuran (**2e**) and 4-iodoacetophenone (**3b**) (microwave heating, 200 °C, 30 min). $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 1.99 (s, 3H), 2.29 (s, 3H), 2.58 (s, 3H), 6.59 (s, 1H), 7.64 (d, $J$=8.2 Hz, 2H), 7.93 (d, $J$=8.2 Hz, 2H). $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 9.9, 11.6, 26.4, 111.1, 116.8, 122.7, 128.9, 134.8, 135.2, 149.1, 149.7, 197.3. HRMS (ESI-TOF) *m/z* calcd for $C_{14}H_{15}O_2$ $[MH]^+$: 215.1072, found: 215.1073.

*4.4.10. 2-(p-Cyanophenyl)-4,5-dimethylfuran (**4ee**)*

Isolated yield, 66% from 2,3-dimethylfuran (**2e**) and 4-iodobenzonitrile (**3e**) (microwave heating, 150 °C, 30 min). $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 1.99 (s, 3H), 2.29 (s, 3H), 6.59 (s, 1H), 7.59 (d, $J$=8.3 Hz, 2H), 7.63 (d, $J$=8.3 Hz, 2H). $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 9.8, 11.6, 109.1, 111.7, 117.0, 119.2, 123.1, 132.4, 134.9, 148.9, 149.5. HRMS (ESI-TOF) *m/z* calcd for $C_{13}H_{12}NO$ $[MH]^+$: 198.0919, found: 198.0918.

*4.4.11. 3-(p-Acetylphenyl)-1-phenylpyrrole (**4fb**)*

Isolated yield, 58% (86% NMR yield) from 1-phenylpyrrole (**2f**) and 4-iodoacetophenone (**3b**) (microwave heating, 200 °C, 30 min). $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 2.56 (s, 3H), 6.66–6.67 (m, 1H), 7.09–7.11 (m, 1H), 7.24–7.27 (m, 1H), 7.40–7.44 (m, 5H), 7.60 (d, $J$=8.3 Hz, 2H), 7.92 (d, $J$=8.3 Hz, 2H). $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 26.4, 108.8, 117.0, 120.5, 120.9, 124.7, 125.6, 126.1, 129.0, 129.7, 134.4, 140.19, 140.22, 197.5. HRMS (FAB) *m/z* calcd for $C_{18}H_{15}NO$ $[M]^+$: 261.1154, found: 261.1153.

*4.4.12. (p-Acetylphenyl)-1-methylindole (**4gb**, C-3 arylation product)*

Isolated yield, 57%. $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 2.62 (s, 3H), 3.84 (s, 3H), 7.23 (dd, $J$=8.3, 6.8 Hz, 1H), 7.31 (dd, $J$=8.3, 6.8 Hz, 1H), 7.34 (s, 1H), 7.38 (d, $J$=8.3 Hz, 1H), 7.74 (d, $J$=8.3 Hz, 2H), 7.97 (d, $J$=8.3 Hz, 1H), 8.02 (d, $J$=8.3 Hz, 2H). $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 26.5, 33.0, 109.8, 115.5, 119.8, 120.5, 122.3, 125.8, 126.6, 127.6, 129.0, 134.2, 137.7, 140.8, 197.6. HRMS (ESI-TOF) *m/z* calcd for $C_{17}H_{16}NO$ $[MH]^+$: 250.1232, found: 250.1234. **4gb′** (C-2 arylation product): 23% isolated yield. $^1$H NMR (600 MHz, $CDCl_3$) $\delta$ 2.66 (s, 3H), 3.79 (s, 3H), 6.66 (s, 1H), 7.16 (dd, $J$=8.2, 6.8 Hz, 1H), 7.29 (dd, $J$=8.2, 6.8 Hz, 1H), 7.38 (d, $J$=8.2 Hz, 1H), 7.63 (d, $J$=8.3 Hz, 2H), 7.65 (d, $J$=8.2 Hz, 1H), 8.06 (d, $J$=8.3 Hz, 2H). $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$ 26.7, 31.4, 103.0, 109.8, 120.2, 120.8, 122.4, 127.9, 128.6, 129.2, 136.1, 137.4, 138.9, 140.2, 197.6. HRMS (ESI-TOF) *m/z* calcd for $C_{17}H_{16}NO$ $[MH]^+$: 250.1232, found: 250.1224.

### 4.5. Coupling of benzene derivatives and iodoarenes

#### 4.5.1. Arylation of anisole

A 10-mL flame-dried microwave vial containing a magnetic stirring bar was fitted with a septum and cooled under a stream of argon. To this vial were added Rh complex **1** (32.3 mg, 26 μmol), $Ag_2CO_3$ (139.9 mg, 0.51 mmol), anisole (**5**: 1.49 g, 13.8 mmol), and 1-iodo-4-nitrobenzene (**3f**: 128.5 mg, 0.52 mmol). The vial was sealed and heated with stirring at 200 °C for 30 min in a CEM Discover microwave apparatus. After the reaction vial was cooled down to room temperature, the mixture was passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was subjected to gel permeation chromatography ($CHCl_3$) to afford biaryls (58.1 mg, 51%) as a mixture of *para*-isomer (**6**) and *ortho*-isomer (**7**). The ratio of **6**/**7** was determined to be 71:29 by $^1H$ NMR analysis. These isomers could be separated by HPLC (silica gel). *4-Methoxy-4′-nitrobiphenyl* (***6***): $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 3.87 (s, 3H), 7.01 (d, $J$=8.9 Hz, 2H), 7.57 (d, $J$=8.9 Hz, 2H), 7.67 (d, $J$=8.9 Hz, 2H), 8.25 (d, $J$=8.9 Hz, 2H). $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 55.4, 114.6, 124.1, 127.0, 128.5, 131.0, 146.5, 147.1, 160.4. HRMS (FAB) *m/z* calcd for $C_{13}H_{11}NO_3$ $[M]^+$: 229.0739, found: 229.0739. *4′-Methoxy-2-nitrobiphenyl* (***7***): $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 3.80 (s, 3H), 6.98 (d, $J$=8.3 Hz, 1H), 7.03 (t, $J$=7.6 Hz, 1H), 7.29 (d, $J$=7.6 Hz, 1H), 7.36 (dd, $J$=8.3, 7.6 Hz, 1H), 7.65 (d, $J$=8.9 Hz, 2H), 8.21 (d, $J$=8.9 Hz, 2H). $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 55.6, 111.4, 121.1, 123.2, 128.2, 130.1, 130.3, 130.6, 145.4, 146.6, 156.4. HRMS (FAB) *m/z* calcd for $C_{13}H_{11}NO_3$ $[M]^+$: 229.0739, found: 229.0739.

#### 4.5.2. Arylation of 1,3-dimethoxybenzene

A 10-mL flame-dried microwave vial containing a magnetic stirring bar was fitted with a septum and cooled under a stream of argon. To this vial were added Rh complex **1** (31.5 mg, 26 μmol), $Ag_2CO_3$ (139.7 mg, 0.51 mmol), 1,3-dimethoxybenzene (**8**: 1.90 g, 13.7 mmol), and 1-iodo-4-nitrobenzene (**3f**: 127.5 mg, 0.50 mmol). The vial was sealed and heated with stirring at 200 °C for 30 min in a CEM Discover microwave apparatus. After the reaction vial was cooled down to room temperature, the mixture was passed through a short silica gel pad (EtOAc). The filtrate was evaporated and the residue was subjected to gel permeation chromatography ($CHCl_3$) to afford **9** (98.5 mg, 76%) as pale yellow solid. *2,4-Dimethoxy-4′-nitrobiphenyl* (***9***): $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 3.82 (s, 3H), 3.86 (s, 3H), 6.58 (d, $J$=2.1 Hz, 1H), 6.59 (dd, $J$=8.4, 2.1 Hz, 1H), 7.26 (d, $J$=8.4 Hz, 1H), 7.65 (d, $J$=8.9 Hz, 2H), 8.21 (d, $J$=8.9 Hz, 2H). $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 55.4, 55.5, 99.0, 105.1, 121.0, 123.2, 129.9, 131.3, 145.3, 146.1, 157.5, 161.5. HRMS (FAB) *m/z* calcd for $C_{14}H_{13}NO_4$ $[M]^+$: 259.0845, found: 259.0847.

### 4.6. Synthesis of extended π-systems through multiple C–H coupling

#### 4.6.1. 5,5′-(1,3-Phenylene)bis(2-ethylthiophene) (11)

A 10-mL flame-dried microwave vial containing a magnetic stirring bar was fitted with a septum and cooled under a stream of argon. To this vial were added Rh complex **1** (30.3 mg, 25 μmol), $Ag_2CO_3$ (220.1 mg, 0.80 mmol), 2-ethylthiophene (**2c**: 224.7 mg, 2.0 mmol), 1,3-diiodobenzene (**10**: 133.3 mg, 0.40 mmol), and dry *m*-xylene (2.5 mL). The vial was sealed and heated with stirring at 150 °C for 30 min in a CEM Discover microwave apparatus. After the reaction vial was cooled down to room temperature, the mixture was passed through a pad of Celite® with copious washing with $CHCl_3$. The filtrate was evaporated and the residue was subjected to gel permeation chromatography ($CHCl_3$) to afford **11** (74.5 mg, 62%) as pale yellow oil. $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 1.33 (t, $J$=7.6 Hz, 6H), 2.85 (q, $J$=7.6 Hz, 4H), 6.75 (d, $J$=3.8 Hz, 2H), 7.15 (d, $J$=3.8 Hz, 2H), 7.31 (t, $J$=7.6 Hz, 1H), 7.42 (dd, $J$=7.6, 2.0 Hz, 2H), 7.73 (t, $J$=2.0 Hz, 1H). $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 15.9, 23.6, 122.6, 123.0, 124.2, 124.3, 129.2, 135.3, 141.2, 147.4. HRMS (ESI-TOF) *m/z* calcd for $C_{18}H_{19}S_2$ $[MH]^+$: 299.0928, found: 299.0927.

#### 4.6.2. 5,5′-(1,4-Phenylene)bis(2-ethylthiophene) (13)

A 10-mL flame-dried microwave vial containing a magnetic stirring bar was fitted with a septum and cooled under a stream of argon. To this vial were added Rh complex **1** (30.4 mg, 25 μmol), $Ag_2CO_3$ (225.7 mg, 0.82 mmol), 2-ethylthiophene (**2c**: 224.7 mg, 2.0 mmol), 1,4-diiodobenzene (**12**: 132.8 mg, 0.40 mmol), and dry *m*-xylene (2.5 mL). The vial was sealed and heated with stirring at 150 °C for 30 min in a CEM Discover microwave apparatus. After the reaction vial was cooled down to room temperature, the mixture was passed through a pad of Celite® with copious washing with $CHCl_3$. The filtrate was evaporated and the residue was subjected to gel permeation chromatography ($CHCl_3$) to afford **13** (56.0 mg, 46%) as pale yellow solid. $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$ 1.34 (t, $J$=7.6 Hz, 6H), 2.87 (q, $J$=7.6 Hz, 4H), 6.76 (d, $J$=3.4 Hz, 2H), 7.13 (d, $J$=3.4 Hz, 2H), 7.53 (s, 4H). $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$ 15.9, 23.6, 122.6, 124.4, 125.7, 133.4, 141.2, 147.2. HRMS (ESI-TOF) *m/z* calcd for $C_{18}H_{19}S_2$ $[MH]^+$: 299.0928, found: 299.0927.

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