JOC The Journal of Organic Chemistry

Article

Selective Monoarylation of Aromatic Ketones via C–H Bond Cleavage by Trialkylphosphine Ruthenium Catalysts

Issei Suzuki, Hikaru Kondo, Takuya Kochi, and Fumitoshi Kakiuchi

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.9b01756 • Publication Date (Web): 19 Sep 2019

Just Accepted

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

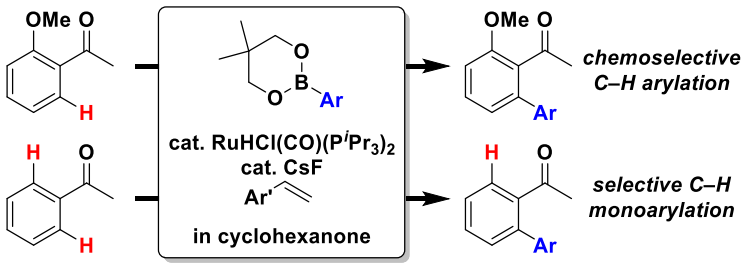
Selective Monoarylation of Aromatic Ketones via C–H Bond Cleavage by Trialkylphosphine Ruthenium Catalysts

Issei Suzuki, Hikaru Kondo, Takuya Kochi, and Fumitoshi Kakiuchi*

Department of Chemistry, Faculty of Science and Technology, Keio University, 3-14-1 Hiyoshi, Kohoku-ku, Yokohama, Kanagawa 223-8522, Japan.

kakiuchi@chem.keio.ac.jp

Table of Contents/Abstract Graphic



Abstract

A catalyst system consisting of RuHCl(CO)(P^{i}Pr$_3$)$_2$, CsF, and a styrene derivative was found applicable to selective monoarylation of aromatic ketones via ortho C–H bond cleavage. The reaction of 2'-methoxyacetophenone with arylboronates gave C–H arylation products without cleaving the ortho C–O bond. Acetophenone was also converted to monoarylation products with

high selectivity. Cyclohexanone was found as an effective solvent for the C–H arylation using the catalyst system.

Introduction

Catalytic bond formation via cleavage of unreactive bonds by transition metal complexes have become a powerful tool in organic synthesis, and conversion of diverse types of C–H and C–heteroatom bonds have been achieved using a variety of transition metal catalysts.[1,2] When there are more than one cleavable bond present in substrates, however, selective cleavage of one particular bond and its conversion may be challenging.[3] Our group have reported that $RuH_2(CO)(PPh_3)_3$ can be used as a catalyst for various types of arylation of aromatic ketones with arylboronates via cleavage of ortho C–H, C–O, C–N, and C–F bonds (Figures 1a and 1b),[4-7] but arylation of aromatic ketones having two cleavable bonds at ortho positions generally provides diarylation products (Figure 1c).[5] For this catalyst system, it is considered that after the formation of intermediate **A** by the first cleavage and transformation of a bond at the other ortho position, the second cleavage of a bond at an ortho position to give intermediate **B** is faster than dissociation of monoarylation product **C** from the metal center (Figure 1d). Investigation of methods for selective monoarylation of aromatic ketones was then explored using ruthenium catalysts. For the reaction of aromatic ketones having two ortho C–H bonds, addition of styrene was found to improve the selectivity towards monoarylation (Scheme 1a).[3c] Recently, we also found that selective monoarylation of aromatic ketones bearing two ortho carbon-heteroatom bonds such as C–O and C–N bonds can be achieved using a catalyst system consisting of $RuHCl(CO)(P^iPr_3)_2$, CsF, and styrene (Scheme 1b).[6d] The high selectivity toward monoarylation

prompted us to examine its application to selective monoarylation of other types of aromatic ketones.

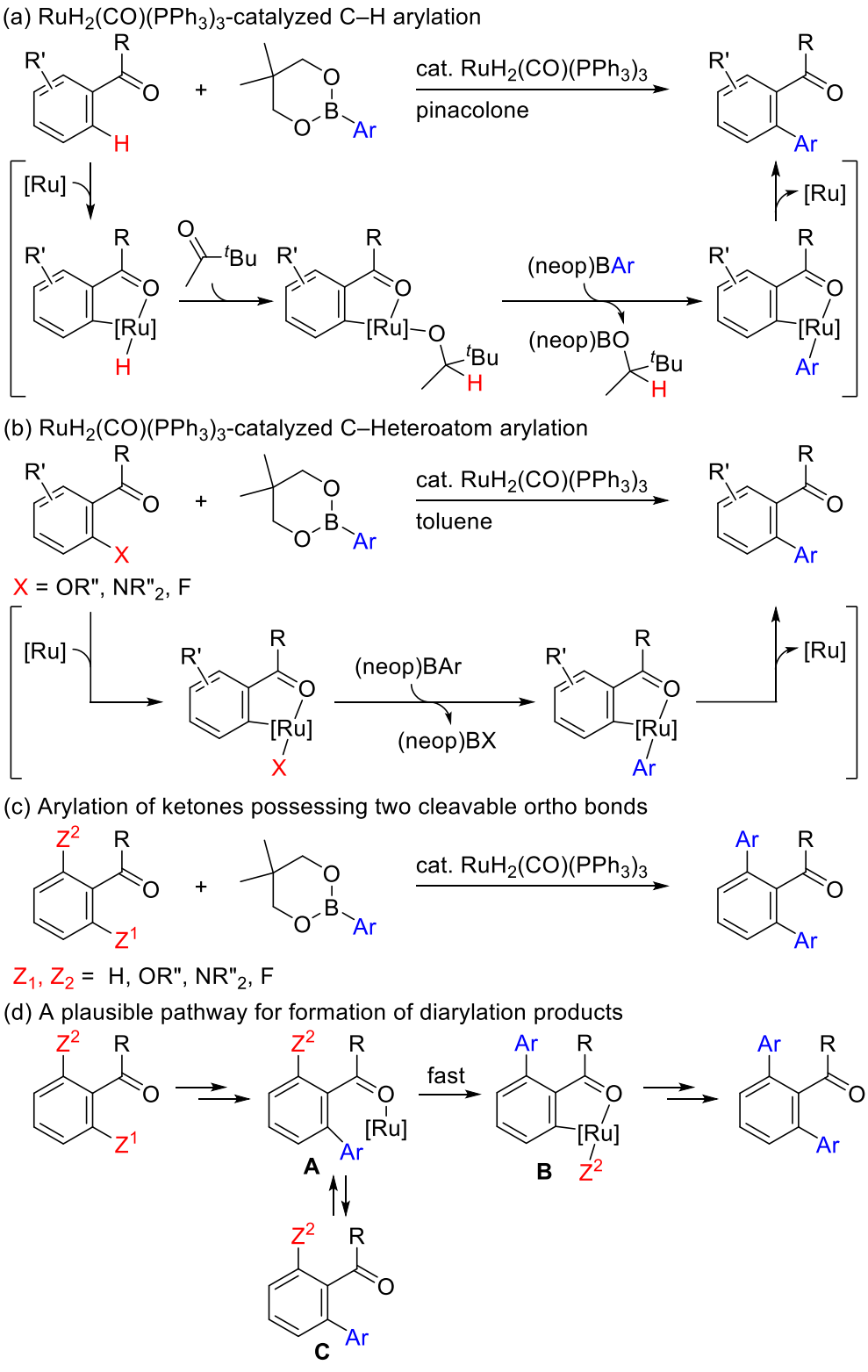
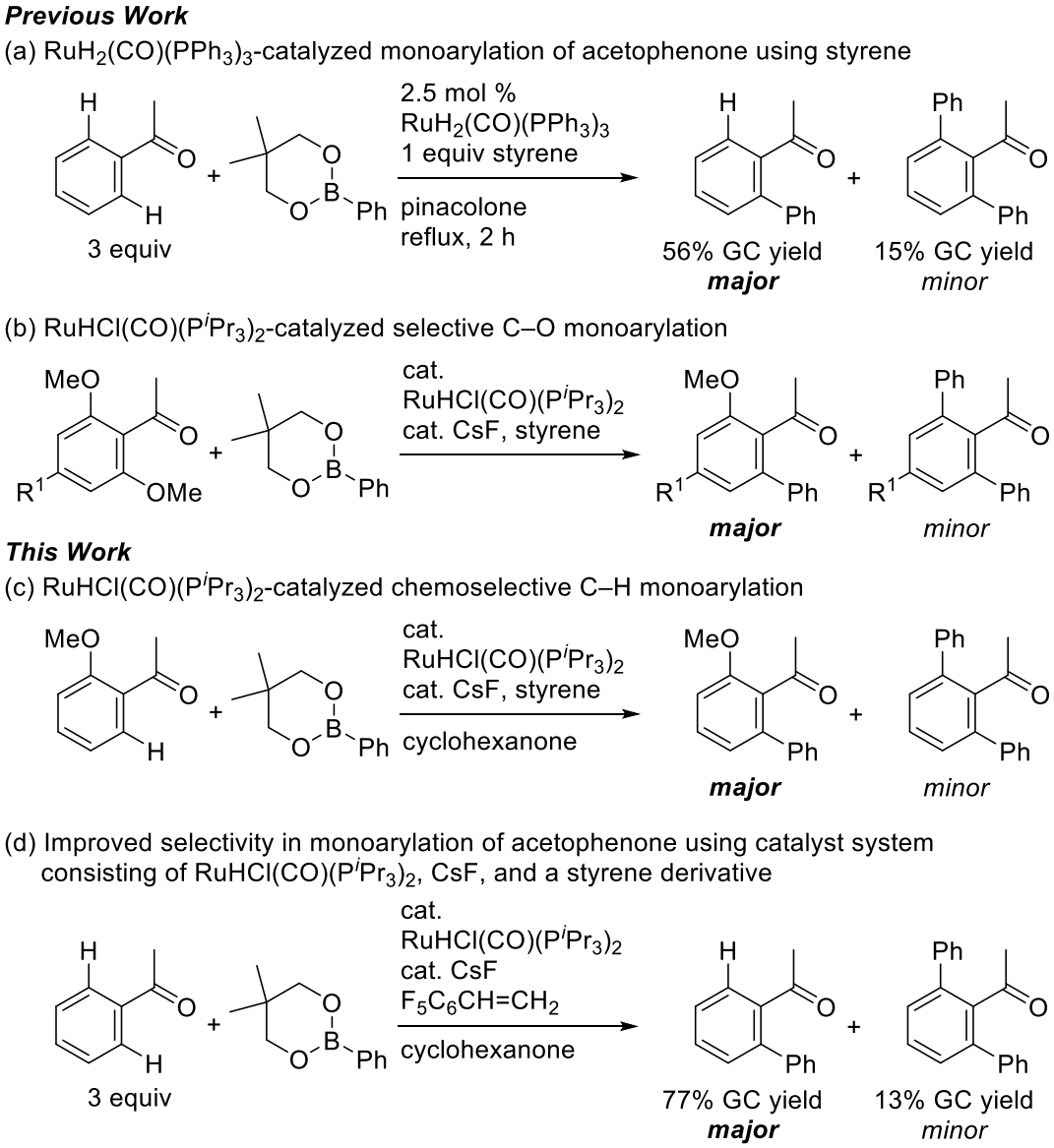


Figure 1. $RuH_2(CO)(PPh_3)_3$-catalyzed ortho-selective arylation of aromatic ketones with arylboronates via C–H and C–heteroatom bond cleavage

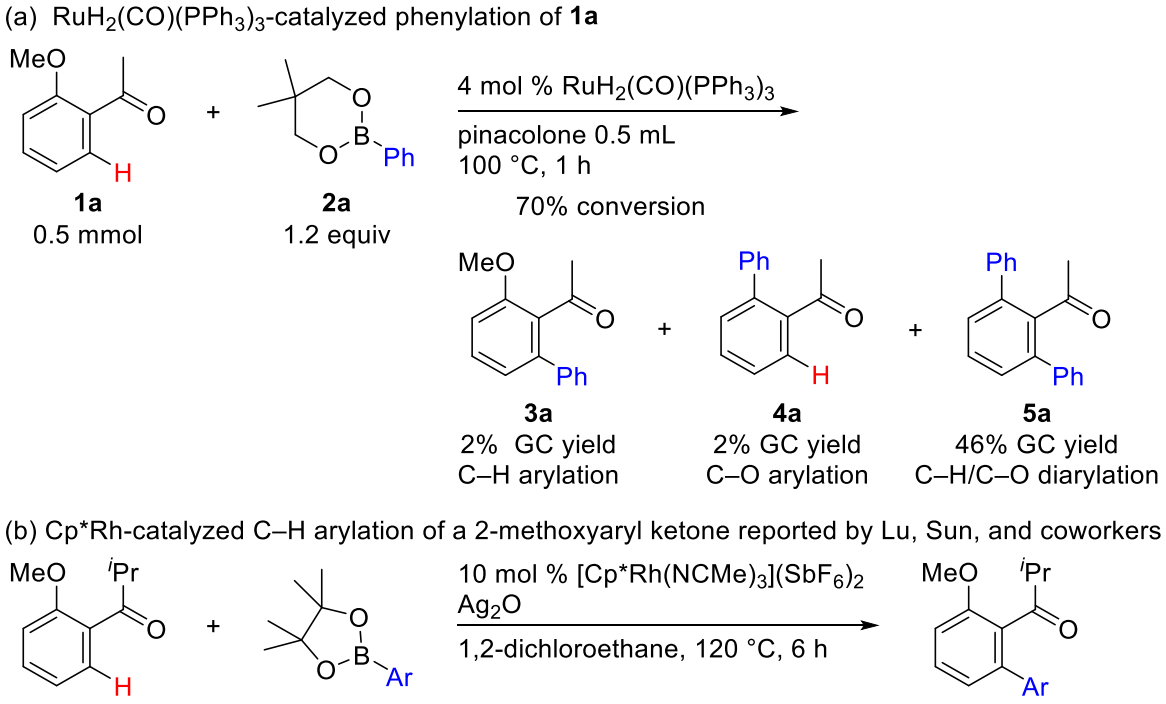


Scheme 1. Ruthenium-catalyzed selective monoarylation of aromatic ketones

Herein we report that selective monoarylation via C–H bond cleavage is achieved for 2'-methoxyacetophenone and acetophenone using catalyst systems consisting of $RuHCl(CO)(P^iPr_3)_2$, CsF, and a styrene derivative. The reaction of 2'-methoxyacetophenone selectively gave the C–H arylation product with maintaining the C–O bond (Scheme 1c). The C–H arylation of acetophenone provided monoarylation products in higher yields than those prepared using the previously-reported catalyst system involving $RuH_2(CO)(PPh_3)_3$ and styrene (Scheme 1d). Cyclohexanone, an inexpensive, relatively high-boiling point solvent, was found as the most suitable solvent for both of the C–H monoarylation reactions using this catalyst system.

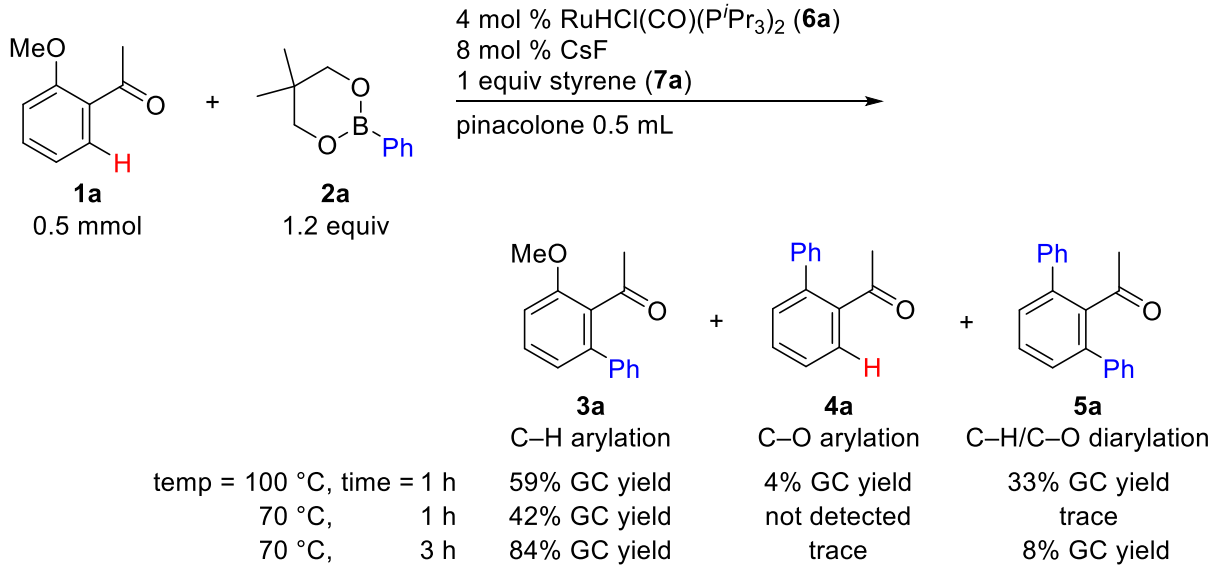
Results and Discussion

The reaction of 2'-methoxyacetophenone **1a** was first examined. Previously, ketone **1a** was used for selective monoalkenylation via ortho C–H bond cleavage using $RuH_2(CO)(PPh_3)_3$ as a catalyst. In the alkenylation, coordination of the alkenyl group in the monoalkenylation product is considered to effectively inhibit the C–O bond cleavage and to suppress the formation of the dialkenylation product. Selective monoarylation of ketone **1a** via C–H bond cleavage was difficult to achieve by using $RuH_2(CO)(PPh_3)_3$ because of the rapid diarylation. For example, when the reaction of **1a** with 1.2 equiv of phenylboronate **2a** was conducted in the presence of 4 mol % of $RuH_2(CO)(PPh_3)_3$ in pinacolone at 100 ºC for 1 h, 46% yield of diarylation product **5a** was obtained as a major product and only small amounts of monoarylation products **3a** and **4a** were observed. (Scheme 2a). Selective C–H arylation of 2-methoxyaryl ketones was reported by Lu, Sun, and coworkers using a Cp*Rh(III) catalyst,[3i] but the examples only included the reaction of ketones having an isopropyl group, and the reactions of acetophenone derivatives were not described (Scheme 2b).



Scheme 2. Catalytic arylations of 2-methoxyaryl ketones

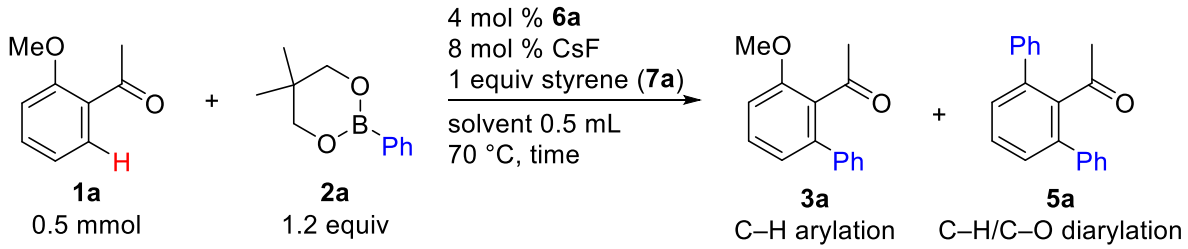
When the reaction of ketone **1a** with 1.2 equiv of phenylboronate **2a** was performed in the presence of 4 mol % of RuHCl(CO)(P^iPr_3)$_2$ (**6a**), 8 mol % of CsF, and 1 equiv of styrene (**7a**) in pinacolone for 1 h at 100 ºC, C–H arylation product **3a** was formed in 59% GC yield along with 4% GC yield of C–O arylation product **4a** and 33% GC yield of C–H/C–O diarylation product **5a** (Scheme 3). In order to improve the selectivity toward **3a**, the reaction conditions were examined. Lowering of the temperature to 70 ºC suppressed the formations of **4a** and **5a** with providing **3a** in 42% GC yield. Extension of the reaction time to 3 h led to the increase of the yield of **3a** to 84%, but the diarylation product **5a** was also obtained in 8% yield. The use of other trialkylphosphine ruthenium complexes, RuHCl(CO)(P^tBu_2Me)$_2$ (**6b**) and RuHCl(CO)(PCy_3)$_2$ (**6c**) as a catalyst resulted in reduction of the yield of **3a**.



Scheme 3. Chemoselective C–H arylation of 2'-methoxyacetophenone (**1a**) with arylboronate **2a** by triisopropylphosphine ruthenium catalyst **6a**

In order to achieve further improvement of the selectivity toward **3a**, ketone solvents, which also function as hydride acceptors, other than pinacolone were examined for the arylation (Table 1). The reactions in various ketones were initially performed for 1 h to compare the catalytic activity and the selectivity before the reaction reached full conversion of **1a**. In all of the ketones shown in Table 1, the reaction gave less than a trace amount of C–O arylation product **4a**. The reaction in acetone gave **3a** in 51% yield with only a trace amount of **5a** (entry 1). The use of 3-methylbutan-2-one slightly improve the yield of **3a** to 56%, but the amount of **5a** was also increased (entry 2), while reduction of the yield to 32% was observed for the reaction in 2-heptanone (entry 3). Examination of cyclic ketones (entries 4-6) showed that cyclohexanone is an effective solvent and provided **3a** in 71% yield with an excellent material balance (entry 5). Introduction of a methyl group at an α-position of cyclohexanone improved the yield of **3a** to 89% with generating **5a** in 3% yield (entry 7), but the reaction in 2,6-dimethylcyclohexanone lowered the yield of **3a** significantly (entry 8). Finally, elongation of the reaction time was investigated for ketone solvents giving promising results such as acetone and cyclohexanone (entries 9 and 10), and the reaction for 3 h in cyclohexanone was found to provide **3a** in 92% GC yield (entry 10).

Table 1. Screening of Solvents for Chemoselective C–H Arylation of 1a with 2a by Catalyst 6a[a]

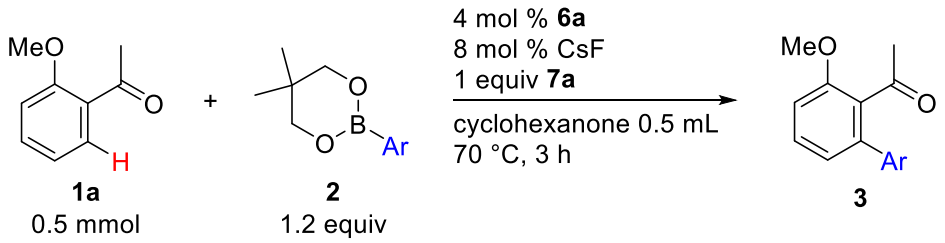


Entry	solvent	time (h)	conversion of **1** (%)	GC yield (%)	
				3a	**5a**
1	acetone	1	59	51	trace
2	3-methylbutan-2-one	1	68	56	1
3	2-heptanone	1	42	32	trace
4	cyclopentanone	1	32	27	trace
5	cyclohexanone	1	73	71	trace
6	cycloheptanone	1	31	20	nd[b]
7	2-methylcyclohexanone	1	97	89	3
8	2,6-dimethylcyclohexanone	1	53	38	trace
9	acetone	3	92	88	1
10	cyclohexanone	3	96	92	2

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), **6a** (0.02 mmol), CsF (0.04 mmol), **7a** (0.5 mmol), solvent (0.5 mL), 70 ºC. [b]Not detected.

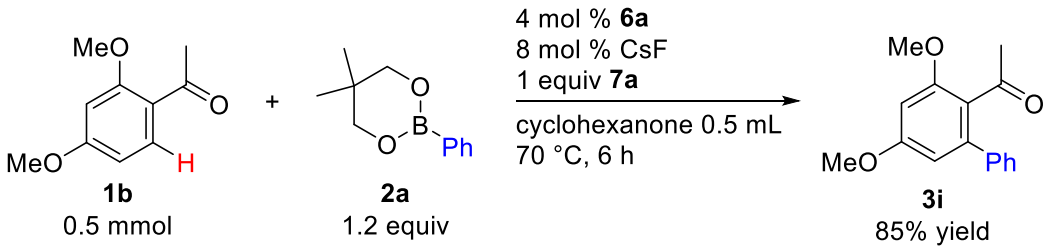
The chemoselective C–H arylation of **1a** was applicable to various arylboronates and monoarylation products were isolated in high yields (Table 2). Phenylation product **3a** was first conducted and obtained in 88% yield (entry 1). The reaction with arylboronates possessing electron-donating groups including dimethylamino (**2b**), methoxy (**2c**), and methyl (**2d**) groups at the para position gave the corresponding C–H arylation products **3b-d** in 80-94% yields (entries 2-4). The arylation can be performed with arylboronates possessing a halogeno group such as bromo (**2e**) and chloro (**2f**) groups to provide **3e** and **3f** in high yields (entries 5 and 6). The reaction also proceeded with 4-trifluoromethylphenylboronate **2g** to afford biaryl **3g** in 78% yield (entry 7). 2-Naphthylboronate **2h** can also be used for the C–H arylation to give **3h** in 81% yield (entry 8). The C–H arylation was also conducted using 2',4'-dimethoxyacetophenone **1b** and phenylboronate **2a** and the corresponding C–H phenylation product **3i** was obtained in 85% yield (Scheme 4). The reaction of 2'-(*N*,*N*-dimethylamino)acetophenone was also examined but gave a complex mixture of products including the corresponding monoarylation and diarylation products.

Table 2. Chemoselective C–H Arylation of 1a with Various Arylboronates 2 by Catalyst 6a[a]



entry	2	Ar	3	yield (%)
1	**2a**	Ph	**3a**	88
2[b]	**2b**	4-$Me_2NC_6H_4$	**3b**	80
3	**2c**	4-$MeOC_6H_4$	**3c**	94
4	**2d**	4-MeC_6H_4	**3d**	89
5	**2e**	4-ClC_6H_4	**3e**	83
6	**2f**	4-BrC_6H_4	**3f**	91
7	**2g**	4-$F_3CC_6H_4$	**3g**	78
8	**2h**	2-naphthyl	**3h**	81

[a]Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), **6a** (0.02 mmol), CsF (0.04 mmol), **7a** (0.5 mmol), cyclohexanone (0.5 mL). [b] Performed for 18 h.

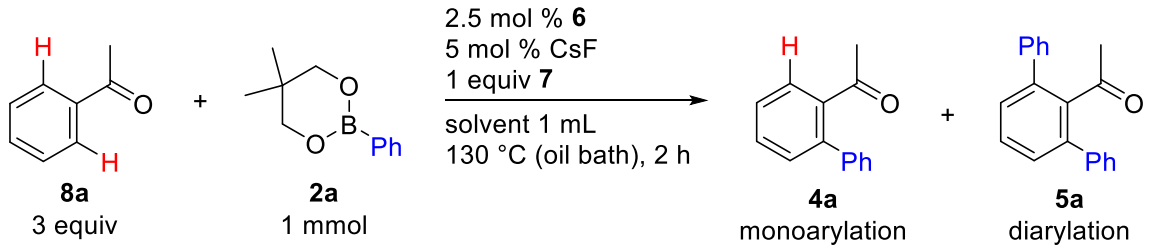


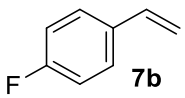
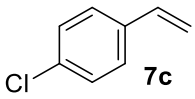
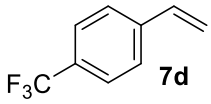
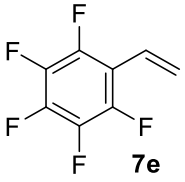
Scheme 4. Chemoselective C–H phenylation of 2',4'-dimethoxyacetophenone (**1b**)

Selective C–H monoarylation of parent acetophenone **8a** was then investigated. The reaction was previously examined using $RuH_2(CO)(PPh_3)_3$ as a catalyst and styrene as an additive, and when arylboronate **2a** was reacted with 3 equiv of **8a**, monoarylation product **4a** was obtained in 56% yield along with diarylation product **5a** (Scheme 1a). Therefore, the monoarylation was examined using a 3:1 ratio of ketone **8a** and arylboronate **2a** in the presence of trialkylphosphine ruthenium complex, CsF, and styrene derivatives to compare the results with the previous catalyst system.

When the reaction was examined using 2.5 mol % of catalyst **6a**, 5 mol % of CsF, and 1 equiv of **7a** in pinacolone for 2 h at 130 ºC (oil bath temp), monoarylation product **4a** was formed in 70% GC yield, which is already higher than the previous catalyst system (Scheme 1a), along with 8% GC yield of diarylation product **5a** (Table 3, entry 1). Catalysts **6b** and **6c** were then tested for the reaction but resulted in lower yields (entries 2 and 3). Because the use of cyclohexanone improved the material balance between substrate **1a** and arylation products **3a** and **5a** in the C–H arylation (Table 1, entry 10), the phenylation of **8a** was examined in cyclohexanone. As a result, monoarylation product **4a** was obtained in slightly lower yield (65%), but the material balance between substrate **8a** and products **4a** and **5a** was again improved (entry 4). In order to enhance the π-accepting ability, introduction of electronegative substituents was also explored, and it was found that the yield of **4a** was affected by introduction of electronegative substituents on the styrene additive (entries 5-8). Particularly, the reaction in the presence of 4-trifluoromethylstyrene (**7d**) or 2,3,4,5,6-pentafluorostyrene (**7e**) provided monoarylation product **4a** in 77% yield (entries 7 and 8). Since the reaction using **7e** gave slightly less diarylation product **5a** than that using **7d**, further examination of the reaction was conducted using **7e** as an additive.

Table 3. Selective C–H Monoarylation of Acetophenone (8a) with 2a by Trialkylphosphine Ruthenium Catalysts 6[a]

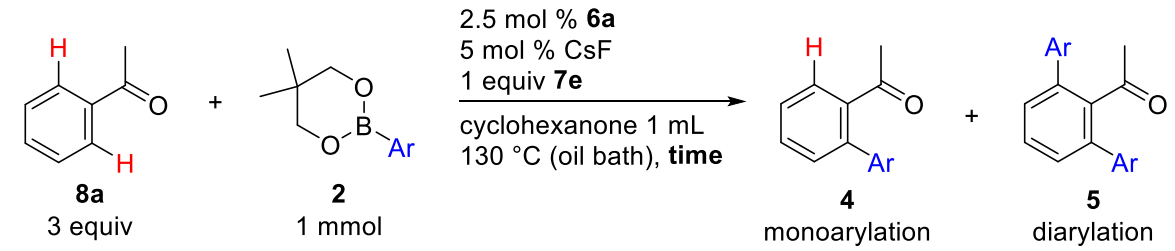


entry	$RuHCl(CO)(PR_3)_2$ **6**	styrene **7**	solvent	conversion of **8** (%)	GC yields (%)	
					4a	**5a**
1	**6a** ($PR_3 = P^iPr_3$)	**7a**	pinacolone	>99	70	8
2	**6b** ($PR_3 = P^tBu_2Me$)	**7a**	pinacolone	63	51	6
3	**6c** ($PR_3 = PCy_3$)	**7a**	pinacolone	87	60	6
4	**6a**	**7a**	cyclohexanone	>99	65	30
5	**6a**	 **7b**	cyclohexanone	>99	60	34
6	**6a**	 **7c**	cyclohexanone	>99	69	23
7	**6a**	 **7d**	cyclohexanone	99	77	15
8	**6a**	 **7e**	cyclohexanone	97	77	13

[a]Reaction conditions: **8a** (3 mmol), **2a** (1 mmol), **6** (0.025 mmol), CsF (0.05 mmol), **7** (1 mmol), solvent (1 mL), 130 ºC.

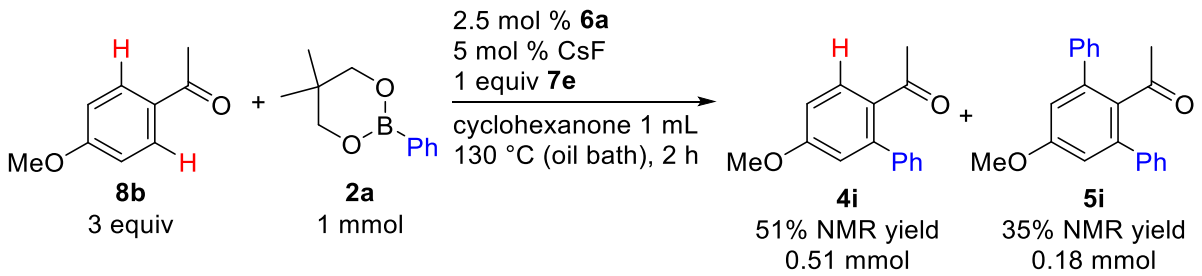
The improved conditions for C–H monoarylation was applied to the reaction with various arylboronates (Table 4). The reactions with **2b-2d** were not completed in 2 h, but elongation of the reaction time to 4 h led to the formation of the corresponding monoarylation products **4b-4d** in 67-74% isolated yields (entries 1-3). The reaction with 4-fluoro-, 4-chloro-, and 4-bromophenylboronates (**2j** , **2e**, and **2f**) also monoarylation products **4j**, **4e**, and **4f** as major products as well, but the mono-/diarylation ratios were decreased as the electron-withdrawing ability of the 4-substituent increased (entries 4-6). The arylation of **8a** with 4-trifluoromethylboronate **2g** also proceeded to give 56% yield of monoarylation product **4g** and 28% yield of diarylation product **5g** (entry 7). It is worth noting that using this catalyst system, monoarylation products **4** were generally obtained in higher yields than the previous systems employing $RuH_2(CO)(PPh_3)_3$ and styrene (71% isolated yields for **4b**, 67% isolated yield for **4c**, 41% GC yield for **4j**, and 33% GC yield for **4g**). The reaction was applicable to the introduction of the 2-naphthyl group and afforded **4h** and **5h** in 69 and 19% yields, respectively (entry 8). The C–H arylation was also conducted using 4'-methoxyacetophenone **8b** and phenylboronate **2a** (Scheme 5). The mono/diarylation selectivity was lowered in this case, and the corresponding C–H monophenylation product **4i** was obtained in 51% NMR yield along with 35% NMR yield of diphenylation product **5i**.

Table 4. Selective C–H Monoarylation of 8a with Various Arylboronates 2 by Catalyst 6a[a]



Entry	2	Ar	time (h)	yields (%)	
				4	5
1	**2b**	4-$Me_2NC_6H_4$	4	74 (**4b**)	nd[b] (**5b**)
2	**2c**	4-$MeOC_6H_4$	4	74 (**4c**)	12 (**5c**)
3	**2d**	4-MeC_6H_4	4	67 (**4d**)	15 (**5d**)
4	**2j**	4-FC_6H_4	2	67 (**4j**)	20 (**5j**)
5	**2e**	4-ClC_6H_4	2	66 (**4e**)	25 (**5e**)
6	**2f**	4-BrC_6H_4	2	46 (**4f**)	22 (**5f**)
7	**2g**	4-$F_3CC_6H_4$	2	56 (**4g**)	28 (**5g**)
8	**2h**	2-naphthyl	2	69 (**4h**)	19 (**5h**)

[a]Reaction conditions: **8a** (3 mmol), **2a** (1 mmol), **6a** (0.025 mmol), CsF (0.05 mmol), **7e** (1 mmol), cyclohexanone (1 mL), 130 ºC. [b]Not detected.



Scheme 5. C–H arylation of 4'-methoxyacetophenone **8b** with phenylboronate **2a**

Conclusions

In summary, the catalyst system consisting of triisopropylphosphine ruthenium complex **6a**, CsF and a styrene derivative was found to be applicable to chemoselective C–H arylation of *ortho*-methoxylated acetophenones **1** and C–H monoarylation of *ortho*-unsubstituted acetophenones **8**. Various arylboronates were found applicable to the reaction of **1a** to provide the C–H arylation products in high yields with keeping the C–O bond intact. The C–H arylation of **8a** with a variety of arylboronates provided monoarylation products in higher yields than the reaction using the previously-reported $RuH_2(CO)(PPh_3)_3$/styrene catalyst system. Cyclohexanone as a solvent improved the material balance between substrates and was found to be the most suitable solvent for both of the C–H arylation reactions.

Experimental Section

Unless otherwise noted, all reactions were carried out under nitrogen, and commercial reagents were used as received. Aromatic ketones **1a** and **8a** were purchased from Nacalai Tesque, Inc. and dried from $CaCl_2$ and distilled under nitrogen. Aromatic ketones **1b** and **8b** were purchased from Tokyo Chemical Industry Co., Ltd. and Nacalai Tesque, Inc. respectively and recrystallized from hexane prior to use. Arylboronates **2a-d**, **2g, 2h, 2j**,[8] **2e**[9] and **2f**[10] were prepared according to the literature procedures. $RuHCl(CO)(P^iPr_3)_2$ (**6a**),[11] $RuHCl(CO)(P^tBu_2Me)_2$ (**6b**)[12] and $RuHCl(CO)(PCy_3)_2$ (**6c**)[13] were prepared according to the literature procedures. CsF was purchased from Nacalai Tesque, Inc. and used as received. Styrenes **7a-e** were dried from CaH_2 and distilled under nitrogen prior to use. Anhydrous acetone was purchased from FUJIFILM Wako Pure Chemical Corporation and used as received. All ketone solvents except for acetone were dried from $CaSO_4$ and distilled under nitrogen. Styrenes **7a-d** and cyclohexanone were purchased from Nacalai Tesque, Inc. Styrene derivative **7e**, 3-methylbutan-2-one, cyclopentanone, cycloheptanone, 2-methylcyclohexanone, and 2,6-dimethylcyclohexanone were purchased from Tokyo Chemical Industry Co., Ltd. Pinacolone was purchased from FUJIFILM Wako Pure Chemical Corporation. 2-Heptanone was purchased from Kanto Chemical Co. Inc. ^1H NMR spectra were recorded on a JEOL ECX-400, AL-400, or ALPHA-400 spectrometer. GC analysis was performed using a Shimazu GC-2014 equipped with a CBP-10 capillary column (25 m × 0.22 mm, film thickness 0.25 μm). The temperature for GC analysis was programmed from 70 to 250 °C at 10 °C/min ramp with a final hold time of 30 min (injection temperature, 250 °C; detector temperature, 250 °C). Flash chromatography was carried out with aluminium oxide 90 active basic (Merck Millipore), silica gel 60N (Kanto Chemical Co., Inc.), or using an EPCLC-AI-580S (Yamazen Corporation) with silica gel 40 μm.

Optimization of Reaction Conditions for Chemoselective C–H Arylation of 2'-Methoxyacetophenone (1a) with Arylboronate 2a by Trialkylphosphine Ruthenium Catalyst 6. Ruthenium complex **6** (0.02 mmol, 4 mol %) and phenylboronate **2a** (114 mg, 0.6 mmol, 1.2 equiv) were placed in an oven-dried sealed tube containing a magnetic stirring bar and the tube was transferred into the glove box. CsF (6 mg, 0.04 mmol, 8 mol %), 2'-methoxyacetophenone **1a** (75 mg, 0.5 mmol), styrene **7a** (52 mg, 0.5 mmol, 1 equiv) and 0.5 mL of the ketone solvent were added to the mixture. After taken out of the glove box, the mixture was stirred at 60-100 ºC using an oil bath for 1-24 h. The mixture was then cooled to room temperature and volatile materials were removed by rotary evaporation. *n*-Hexadecane was added as an internal standard to the mixture, which was then dissolved in AcOEt. The yield was determined by gas chromatography (GC). The crude material was passed through a basic aluminium oxide column to remove the remaining arylboronate. Further purification of the product was performed by silica gel column chromatography.

General Procedure A for Chemoselective C–H Arylation of 1 with Various Arylboronates 2 by Catalyst 6a. $RuHCl(CO)(P^iPr_3)_2$ **6a** (10 mg, 0.02 mmol, 4 mol %) and arylboronate **2** (0.6 mmol, 1.2 equiv) were placed in an oven-dried sealed tube containing a magnetic stirring bar and the tube was transferred into the glove box. CsF (6 mg, 0.04 mmol, 8 mol %), 2'-methoxyacetophenone **1a** or 2',4'-dimethoxyacetophenone **1b** (0.5 mmol), styrene **7a** (52 mg, 0.5 mmol, 1 equiv) and 0.5 mL of cyclohexanone were added to the mixture. After taken out of the glove box, the mixture was stirred at 70 ºC using an oil bath for 3-18 h. The mixture was then cooled to room temperature and volatile materials were removed by rotary evaporation. The crude material was passed through a basic aluminium oxide column to remove the remaining arylboronate. Further purification of the product was performed by silica gel column

chromatography. ^{1}H NMR spectra of the isolated products were in good agreement with those reported in literature.

*1-(3-Methoxy-[1,1'-biphenyl]-2-yl)ethan-1-one (**3a**)*.[6d] General Procedure A was followed with **1a** (74.7 mg, 0.497 mmol) and **2a** (115.5 mg, 0.608 mmol). Silica gel column chromatography (hexane:AcOEt = 20:1) afforded 99.3 mg of **3a** (0.439 mmol, 88% yield) as a white solid.

*1-(4'-[Dimethylamino]-3-methoxy-[1,1'-biphenyl]-2-yl)ethan-1-one (**3b**)*.[6d] General Procedure A (stirred for 18 h) was followed with **1a** (74.3 mg, 0.495 mmol) and **2b** (139.5 mg, 0.598 mmol). Silica gel column chromatography (hexane:AcOEt = 5:1) afforded 107 mg of **3b** (0.395 mmol, 80% yield) as a white solid.

*1-(3,4'-Dimethoxy-[1,1'-biphenyl]-2-yl)ethan-1-one (**3c**)*.[6d] General Procedure A was followed with **1a** (74.9 mg, 0.492 mmol) and **2c** (133.8 mg, 0.608 mmol). Silica gel column chromatography (hexane:AcOEt = 10:1) afforded 119 mg of **3c** (0.464 mmol, 94% yield) as a white solid.

*1-(3-Methoxy-4'-methyl-[1,1'-biphenyl]-2-yl)ethan-1-one (**3d**)*.[6d] General Procedure A was followed with **1a** (73.6 mg, 0.490 mmol) and **2d** (124.1 mg, 0.608 mmol). Silica gel column chromatography (hexane:AcOEt = 20:1) afforded 105 mg of **3d** (0.435 mmol, 89% yield) as a white solid.

*1-(4'-Chloro-3-methoxy-[1,1'-biphenyl]-2-yl)ethan-1-one (**3e**)*.[6d] General Procedure A was followed with **1a** (74.8 mg, 0.498 mmol) and **2e** (133.3 mg, 0.593 mmol). Silica gel column chromatography (hexane:AcOEt = 10:1) afforded 108 mg of 3**e** (0.416 mmol, 83% yield) as a white solid.

*1-(4'-Bromo-3-methoxy-[1,1'-biphenyl]-2-yl)ethan-1-one (**3f**).*[6d] General Procedure A was followed with **1a** (75.4 mg, 0.502 mmol) and **2f** (160.8 mg, 0.598 mmol). Silica gel column chromatography (hexane:AcOEt = 10:1) afforded 140 mg of **3f** (0.457 mmol, 91% yield) as a white solid.

*1-(3-Methoxy-4'-[trifluoromethyl]-[1,1'-biphenyl]-2-yl)ethan-1-one (**3g**).*[6d] General Procedure A was followed with **1a** (75.6 mg, 0.503 mmol) and **2g** (155.4 mg, 0.602 mmol). Silica gel column chromatography (hexane:AcOEt = 10:1) afforded 115 mg of **3g** (0.392 mmol, 78% yield) as a white solid.

*1-(2-Methoxy-6-(naphthalen-2-yl)phenyl)ethan-1-one (**3h**).*[6d] General Procedure A was followed with **1a** (78.0 mg, 0.519 mmol) and **2h** (145.8 mg, 0.607 mmol). Silica gel column chromatography (hexane:AcOEt = 10:1) afforded 116 mg of **3h** (0.420 mmol, 81% yield) as a white solid.

*1-(3,5-Dimethoxy-[1,1'-biphenyl]-2-yl)ethan-1-one (**3i**).*[6d] General Procedure A was followed with **1b** (90.4 mg, 0.502 mmol) and **2b** (115 mg, 0.605 mmol) and the reaction was performed for 6 h. Silica gel column chromatography (hexane:AcOEt = 92:8), followed by Kugelrohr distillation, afforded 109 mg of **3i** (0.427 mmol, 85 % yield) as a white solid.

Optimization of Reaction Conditions for Selective C–H Monoarylation of Acetophenone 8a with Arylboronate 2a by Triisopropylphosphine Ruthenium Catalyst 6a. $RuHCl(CO)(P^iPr_3)_2$ **6a** (12 mg, 0.025 mmol, 2.5 mol %) and arylboronate **2a** (190 mg, 1 mmol) were placed in an oven-dried 10 mL Schlenk flask containing a magnetic stirring bar and the tube was transferred into the glove box. CsF (8 mg, 0.05 mmol, 5 mol %), acetophenone **8a** (360 mg, 3 mmol, 3 equiv), styrene derivative **7** (1 mmol, 1 equiv) and 1 mL of the ketone solvent were added to the mixture. After taken out of the glove box, the mixture was stirred at 130 °C

using an oil bath for 2-6 h. The mixture was then cooled to room temperature and volatile materials were removed by rotary evaporation. *n*-Hexadecane was added as an internal standard to the mixture, which was then dissolved in AcOEt. The yield was determined by gas chromatography (GC). The crude material was passed through a basic aluminium oxide column to remove the remaining arylboronate. Further purification of the product was performed by silica gel column chromatography.

General Procedure B for Selective C–H Monoarylation of Acetophenone 8 with Arylboronate 2 by Triisopropylphosphine Ruthenium Catalyst 6a. $RuHCl(CO)(P^iPr_3)_2$ **6a** (12 mg, 0.025 mmol, 2.5 mol %) and arylboronates **2** (1 mmol) were placed in an oven-dried 10 mL Schlenk flask containing a magnetic stirring bar and the tube was transferred into the glove box. CsF (8 mg, 0.05 mmol, 5 mol %), acetophenone **8a** or 4'-methoxyacetophenone **8b** (3 mmol, 3 equiv), styrene derivative **7e** (194 mg, 1 mmol, 1 equiv) and 1 mL of ketone solvent were added to the mixture. The mixture was then stirred at 130 °C using an oil bath for 2-4 h. The mixture was then cooled to room temperature and volatile materials were removed by rotary evaporation. The crude material was passed through a basic aluminium oxide column to remove the remaining arylboronate. Further purification of the product was performed by silica gel column chromatography.

*1-(4'-[Dimethylamino]-[1,1'-biphenyl]-2-yl)ethan-1-one (**4b**).* General Procedure B was followed with **8a** (363 mg, 3.02 mmol) and **2b** (235 mg, 1.01 mmol) and the reaction was performed for 4 h. Silica gel column chromatography (hexane:AcOEt = 10:1) afforded 179 mg of **4b** (0.748 mmol, 74% yield) as a yellow oil. The ^{1}H NMR spectrum of **4b** was in good agreement with that reported in literature.[14]

1-(4'-Methoxy-[1,1'-biphenyl]-2-yl)ethan-1-one ***(4c)*** *and 1-(4,4''-dimethoxy-[1,1':3',1''-terphenyl]-2'-yl)ethan-1-one* ***(5c)***. General Procedure B was followed with **8a** (361 mg, 3.00 mmol) and **2c** (221 mg, 1.00 mmol) and the reaction was performed for 4 h. Silica gel column chromatography (hexane:AcOEt = 20:1) afforded 168 mg of **4c** (0.744 mmol, 74% yield) as a colorless oil and 19.9 mg of **5c** (0.0599 mmol, 12% yield) as a white solid. The ^{1}H NMR spectra of **4c**[15] and **5c**[14] were in good agreement with those reported in literature.

1-(4'-Methyl-[1,1'-biphenyl]-2-yl)ethan-1-one ***(4d)*** *and 1-(4,4''-dimethyl-[1,1':3',1''-terphenyl]-2'-yl)ethan-1-one* ***(5d)***. General Procedure B was followed with **8a** (371 mg, 3.08 mmol) and **2d** (206 mg, 1.01 mmol) and the reaction was performed for 4 h. Silica gel column chromatography (toluene:hexane:AcOEt = 40:20:1) afforded 142 mg of **4d** (0.677 mmol, 67% yield) as a colorless oil and 23.2 mg of **5d** (0.0772 mmol, 15% yield) as a white solid. The ^{1}H NMR spectrum of **4d** was in good agreement with that reported in literature.[16] The ^{1}H NMR spectrum of **5d** synthesized here was also in good agreement with that of **5d** prepared by the reaction of **8a** with **2d** using $RuH_2(CO)(PPh_3)_3$ as a catalyst following General Procedure C.

1-(4'-Chloro-[1,1'-biphenyl]-2-yl)ethan-1-one ***(4e)*** *and 1-(4,4''-dichloro-[1,1':3',1''-terphenyl]-2'-yl)ethan-1-one* ***(5e)***. General Procedure B was followed with **8a** (368 mg, 3.06 mmol) and **2e** (244 mg, 1.00 mmol) and the reaction was performed for 2 h. Silica gel column chromatography (hexane:AcOEt = 96:4) afforded 153 mg of **4e** (0.662 mmol, 66% yield) as a colorless oil and 43.2 mg of **5e** (0.127 mmol, 25% yield) as a white solid. The ^{1}H NMR spectrum of **4e** was in good agreement with that reported in literature.[17] Diarylation product **5e**: mp 180-182 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.87 (s, 3 H), 7.27-7.50 (m, 10H), 7.49 (t, J = 8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 33.0, 128.6, 128.9, 129.4, 130.4, 134.0, 137.8, 138.5, 141.1, 205.9; IR (KBr): 3745 w, 1698 s, 1594 w, 1492 s, 1449 m, 1397 m, 1351 m, 1244 m, 1179 w,

1090 s, 1015 m, 850 m, 826 s, 763 m, 605 w, 532 m, 515 m cm^{-1}; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{20}H_{14}Cl_2NaO^+$ 363.0314, found 363.0315.

*1-(4'-Bromo-[1,1'-biphenyl]-2-yl)ethan-1-one (**4f**) and 1-(4,4''-dibromo-[1,1':3',1''-terphenyl]-2'-yl)ethan-1-one (**5f**).* General Procedure B was followed with **8a** (362 mg, 3.01 mmol) and **2f** (267 mg, 0.994 mmol) and the reaction was performed for 2 h. Silica gel column chromatography (toluene:hexane:AcOEt = 20:20:1) afforded 127 mg of **4f** (0.461 mmol, 46% yield) as a colorless oil and 46.8 mg of **5f** (0.109 mmol, 22% yield) as a white solid. The ^1H NMR spectrum of **4f** was in good agreement with that reported in literature.[18] The ^1H NMR spectrum of **5f** synthesized here was also in good agreement with that of **5f** prepared by the reaction of **8a** with **2f** using $RuH_2(CO)(PPh_3)_3$ as a catalyst following General Procedure C.

*1-(4'-[Trifluoromethyl]-[1,1'-biphenyl]-2-yl)ethan-1-one (**4g**) and 1-(4,4''-bis[trifluoromethyl]-[1,1':3',1''-terphenyl]-2'-yl)ethan-1-one (**5g**).* General Procedure B was followed with **8a** (364 mg, 3.03 mmol) and **2g** (258 mg, 1.00 mmol) and the reaction was performed for 2 h. Silica gel column chromatography (hexane:AcOEt = 30:1) afforded 147 mg of **4g** (0.556 mmol, 56% yield) as a colorless oil and 58.0 mg of **5g** (0.142 mmol, 28% yield) as a white solid. The ^1H NMR spectra of **4g** and **5g** were in good agreement with that reported in literature.[3c]

*1-(2-[Naphthalen-2-yl]phenyl)ethan-1-one (**4h**) and 1-(2,6-di[naphthalen-2-yl]phenyl)ethan-1-one (**5h**).* General Procedure B was followed with **8a** (361 mg, 3.00 mmol) and **2h** (240 mg, 1.00 mmol) and the reaction was performed for 2 h. Silica gel column chromatography (toluene:hexane:AcOEt = 40:20:1) afforded 169 mg of **4h** (0.686 mmol, 69% yield) as a colorless oil and 35.6 mg of **5h** (0.0956 mmol, 19% yield) as a white solid. The ^1H NMR spectrum of **4h** was in good agreement with that reported in literature.[19] The ^1H NMR spectrum

of **5h** synthesized here was also in good agreement with that of **5h** prepared by the reaction of **8a** with **2h** using $RuH_2(CO)(PPh_3)_3$ as a catalyst following General Procedure C.

*1-(5-Methoxy-[1,1'-biphenyl]-2-yl)ethan-1-one (**4i**)* and and *1-(5'-methoxy-[1,1':3',1''-terphenyl]-2'-yl)ethan-1-one (**5i**).* General Procedure B was followed with **8b** (455 mg, 3.03 mmol) and **2a** (192 mg, 1.01 mmol) and the reaction was performed for 2 h. Silica gel column chromatography (hexane:AcOEt = 96:4) afforded 466 mg of a mixture of **4i, 5i** and **8b**. The ^{1}H NMR spectra of the mixture and its comparison with those of **4i**,[20] **5i**,[5a] and **8b**[21] reported in literature suggested that the molar ratio of **4i, 5i** and **8b** is ca. 26:9:100, and the mixture contains 116 mg of **4i** (0.51 mmol, 51% yield) and 54 mg of **5i** (0.18 mmol, 35% yield).

*1-(4'-Fluoro-[1,1'-biphenyl]-2-yl)ethan-1-one (**4j**)* and *1-(4,4''-difluoro-[1,1':3',1''-terphenyl]-2'-yl)ethan-1-one (**5j**).* General Procedure B was followed with **8a** (365 mg, 3.04 mmol) and **2j** (209 mg, 1.01 mmol) and the reaction was performed for 2 h. Silica gel column chromatography (hexane:AcOEt = 30:1) afforded 143 mg of **4j** (0.667 mmol, 67% yield) as a colorless oil and 31.2 mg of **5j** (0.102 mmol, 20% yield) as a white solid. The ^{1}H NMR spectra of **4j**[22] and **5j**[3c] were in good agreement with those reported in literature.

General Procedure C for C–H Diarylation of 8a with Arylboronates 2 Using $RuH_2(CO)(PPh_3)_3$ as a Catalyst. C–H diarylation products **5** were prepared by the reaction of **8a** with **2** in the presence of 2.5 mol % of $RuH_2(CO)(PPh_3)_3$ in pinacolone.[5b] $RuH_2(CO)(PPh_3)_3$ (11.5 mg, 0.0125 mmol, 2.5 mol %) and arylboronates **2** (0.9 mmol, 1.8 equiv) were placed in an oven-dried sealed tube containing a magnetic stirring bar and the tube was transferred into the glove box. Acetophenone **8a** (0.5 mmol), and 0.5 mL of pinacolone were added to the mixture. After taken out of the glove box, the mixture was stirred at 120 ℃ for 16 h. The mixture was then cooled to room temperature and volatile materials were removed by rotary evaporation. The

crude material was passed through a basic aluminium oxide column to remove the remaining arylboronate. Further purification of the product was performed by silica gel column chromatography.

*1-(4,4''-Dimethyl-[1,1':3',1''-terphenyl]-2'-yl)ethan-1-one (**5d**).* General Procedure C was followed with **8a** (60.1 mg, 0.500 mmol) and **2d** (183 mg, 0.895 mmol). Silica gel column chromatography (hexane:AcOEt = 97:3) afforded 18.8 mg of **5d** (0.0626 mmol, 13% yield) as a white solid: mp 136-137 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.88 (s, 3H), 2.38 (s, 6H), 7.19-7.25 (m, 8H), 7.32 (d, *J* = 7.2 Hz, 2H), 7.45 (t, *J* = 7.8 Hz, 1 H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 21.2, 33.0, 128.6, 128.9, 129.0, 129.1, 137.3, 137.4, 138.9, 141.2, 206.6; IR (KBr): 3026 w, 2919 w, 1908 w, 1703 s, 1512 m, 1451 m, 1412 w, 1348 m, 1238 m, 829 m, 800 s, 760 m, 518 s cm^{-1}; HRMS (ESI-TOF) *m/z* $[M + K]^+$ calcd for $C_{22}H_{20}KO^+$ 339.1146, found 339.1144.

*1-(4,4''-Dibromo-[1,1':3',1''-terphenyl]-2'-yl)ethan-1-one (**5f**).* General Procedure C was followed with **8a** (61.2 mg, 0.509 mmol) and **2f** (244 mg, 0.908 mmol). Silica gel column chromatography (hexane:AcOEt = 97:3) afforded 23.4 mg of **5f** (0.0544 mmol, 11% yield) as a white solid: mp 219-220 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.88 (s, 3H), 7.21-7.24 (m, 4H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.48 (t, *J* = 12 Hz, 1H), 7.52-7.55(m, 4H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 33.0, 122.2, 128.9, 129.3, 130.7, 131.6, 137.8, 138.9, 141.0, 205.9; IR (KBr): 3067 w, 2919 w, 1067 w, 1705 s, 1589 w, 1489 m, 1449 m, 1389 m, 1349 w, 1243 m, 1008 m, 941 s, 603 w, 515 m cm^{-1}; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{20}H_{14}Br_2NaO^+$ 452.9283, found 452.9277.

*1-(2,6-Di[naphthalen-2-yl]phenyl)ethan-1-one (**5h**).* General Procedure C was followed with **8a** (64.0 mg, 0.533 mmol) and **2h** (217 mg, 0.903 mmol). Silica gel column chromatography (hexane:AcOEt = 97:3) afforded 105 mg of **5h** (0.282 mmol, 53% yield) as a white solid: mp

159-160 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.87 (s, 3H), 7.47-7.57 (m, 9H), 7.85-7.89 (m, 8H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, 50 °C): δ 32.9, 126.3, 126.5, 127.3, 127.7, 128.0, 128.2, 128.3, 128.7, 129.6, 132.7, 133.3, 137.9, 139.1, 141.9, 205.9; IR (KBr): 3053 m, 2919 w, 1695 s, 1598 w, 1505 w, 1349 m, 1242 m, 1133 w, 963 w, 894 m, 860 m, 823 s, 801 s, 750 s, 613 w, 480 s, 434 m s cm^{-1}; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{28}H_{20}NaO^+$ 395.1406, found 395.1407.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at http://pubs.acs.org.

Additional data and copies of ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra (PDF)

Corresponding Author

*E-mail: kakiuchi@chem.keio.ac.jp

ORCID

Takuya Kochi: 0000-0002-5491-0566

Fumitoshi Kakiuchi: 0000-0003-2605-4675

Notes

The authors declare no competing financial interest.

Acknowledgements

This work was supported in part by JSPS KAKENHI Grant Numbers JP17K19126, JP16H04150 and JP15H05839 (Middle Molecular Strategy). T. K. is also grateful for support by JSPS KAKENHI Grant Number JP18H04271 (Precisely Designed Catalysts with Customized Scaffolding). H.K. is also grateful to the Japan Society for the Promotion of Science (JSPS) for a Research Fellowship for Young Scienetists (JP16J02904).

References and Notes

(1) Recent representative reviews of C–H functionalizations: (a) Sarkar, S. D.; Liu, W.; Kozhushkov, S. I.; Ackermann, L. Weakly Coordinating Directing Groups for Ruthenium(II)-Catalyzed C–H Activation. *Adv. Synth. Catal.* **2014**, *356*, 1461–1479. (b) Huang, Z.; Lim, H. N.; Mo, F.; Young, M. C.; Dong, G. Transition Metal-Catalyzed Ketone-Directed or Mediated C–H Functionalization. *Chem. Soc. Rev.* **2015**, *44*, 7764–7786. (c) Kakiuchi, F.; Kochi, T. Chelation-Assisted Catalytic C–C, C–Si and C–Halogen Bond Formation by Substitution via the Cleavage of C(sp2)–H and C(sp3)–H Bonds. *J. Synth. Org. Chem., Jpn.* **2015**, *73*, 1099-1110. (d) Zhu, R.-Y.; Farmer, M. E.; Chen, Y.-Q.; Yu, J.-Q. A Simple and Versatile Amide Directing Group for C−H Functionalizations. *Angew. Chem., Int. Ed.* **2016**, *55*, 10578–10599.

(2) Representative reviews and accounts for catalytic C–O functionalizations: (a) Li, B.-J.; Yu, D.-G.; Sun, C.-L.; Shi, Z.-J. Activation of "Inert" Alkenyl/Aryl C–O Bond and Its Application in Cross-Coupling Reactions. *Chem. –Eur. J.* **2011**, *17*, 1728–1759. (b) Rosen, B. M.; Quasdorf, K. W.; Wilson, D. A.; Zhang, N.; Resmerita, A.-M.; Garg, N. K.; Percec, V. Nickel-Catalyzed Cross-Couplings Involving Carbon–Oxygen Bonds. *Chem. Rev.* **2011**, *111*, 1346–1416. (c) Mesganaw, T.; Garg, N. K. Ni- and Fe-Catalyzed Cross-Coupling Reactions of Phenol Derivatives. *Org. Process. Res. Dev.* **2013**, *17*, 29–39. (d) Yamaguchi, J.; Muto, K.; Itami, K.

Recent Progress in Nickel-Catalyzed Biaryl Coupling. *Eur. J. Org. Chem.* **2013**, *2013*, 19–30. (e) Cornella, J.; Zarate, C.; Martin, R. Metal-Catalyzed Activation of Ethers via C–O Bond Cleavage: A New Strategy for Molecular Diversity. *Chem. Soc. Rev.* **2014**, *43*, 8081–8097. (f) Su, B.; Cao, Z.-C.; Shi, Z.-J. Exploration of Earth-Abundant Transition Metals (Fe, Co, and Ni) as Catalysts in Unreactive Chemical Bond Activations. *Acc. Chem. Res.* **2015**, *48*, 886–896. (g) Tobisu, M.; Chatani, N. N. Cross-Couplings Using Aryl Ethers via C–O Bond Activation Enabled by Nickel Catalysts. *Acc. Chem. Res.* **2015**, *48*, 1717–1726. (h) Tobisu, M.; Chatani, N. Nickel-Catalyzed Cross-Coupling Reactions of Unreactive Phenolic Electrophiles via C–O Bond Activation. *Top. Curr. Chem.* **2016**, *374*, 1-28. (i) Zarate, C.; van Gemmeren, M.; Somerville, R. J.; Martin, R. Phenol Derivatives. *Adv. Organomet. Chem.* **2016**, *66*, 143-222.

(3) Selected examples of C–H monofunctionalizations: (a) Oi, S.; Fukita, S.; Hirata, N.; Watanuki, N.; Miyano, S.; Inoue, Y. Ruthenium Complex-Catalyzed Direct Ortho Arylation and Alkenylation of 2-Arylpyridines with Organic Halides. *Org. Lett.* **2001**, *3*, 2579–2581. (b) Ackermann, L.; Althammer, A.; Born, R. Catalytic Arylation Reactions by C–H Bond Activation with Aryl Tosylates. *Angew. Chem., Int. Ed.* **2006**, *45*, 2619-2622. (c) Hiroshima, S.; Matsumura, D.; Kochi, T.; Kakiuchi, F. Control of Product Selectivity by a Styrene Additive in Ruthenium-Catalyzed C–H Arylation. *Org. Lett.* **2010**, *12*, 5318-5321. (d) Zhang, X.-S.; Zhu, Q.-L.; Zhang, Y.-F.; Li, Y.-B.; Shi, Z.-J. Controllable Mono-/Dialkenylation of Benzyl Thioethers through Rh-Catalyzed Aryl C–H Activation. *Chem. –Eur. J.* **2013**, *19*, 11898–11903. (e) Kim, H. J.; Ajitha, M. J.; Lee, Y.; Ryu, J.; Kim, J.; Lee, Y.; Jung, Y.; Chang, S. Hydrogen-Bond-Assisted Controlled C–H Functionalization via Adaptive Recognition of a Purine Directing Group. *J. Am. Chem. Soc.* **2014**, *136*, 1132–1140. (f) Zhang, S.-Y.; Li, Q.; He, G.; Nack, W. A.; Chen, G. Pd-Catalyzed Monoselective Ortho-C–H Alkylation of N-Quinolyl Benzamides: Evidence for

Stereoretentive Coupling of Secondary Alkyl Iodides. *J. Am. Chem. Soc.* **2015**, *137*, 531–539. (g) Dastbaravardeh, N.; Toba, T.; Farmer, M. E.; Yu, J.-Q. Monoselective *o*-C–H Functionalizations of Mandelic Acid and *α*-Phenylglycine. *J. Am. Chem. Soc.* **2015**, *137*, 9877–9884. (h) Sarkar, D.; Gulevich, A. V.; Melkonyan, F. S.; Gevorgyan, V. Synthesis of Multisubstituted Arenes via PyrDipSi-Directed Unsymmetrical Iterative C–H Functionalizations. *ACS Catal.* **2015**, *5*, 6792–6801. (i) Zhang, B.; Wang, H.-W.; Kang, Y.-S.; Zhang, P.; Xu, H.-J.; Lu, Y.; Sun, W.-Y. Rhodium-Catalyzed Direct Ortho C–H Arylation Using Ketone as Directing Group with Boron Reagent. *Org. Lett.* **2017**, *19* , 5940–5943.

(4) Kakiuchi, F.; Kochi, T.; Murai, S. Chelation-Assisted Regioselective Catalytic Functionalization of C–H, C–O, C–N and C–F Bonds. *Synlett* **2014**, *25*, 2390–2414.

(5) Selected recent examples of our ruthenium-catalyzed C–H functionalization: (a) Kakiuchi, F.; Kan, S.; Igi, K.; Chatani, N.; Murai, S. A Ruthenium-Catalyzed Reaction of Aromatic Ketones with Arylboronates: A New Method for the Arylation of Aromatic Compounds via C−H Bond Cleavage. *J. Am. Chem. Soc.* **2003**, *125*, 1698–1699. (b) Kakiuchi, F.; Matsuura, Y.; Kan, S.; Chatani, N. A $RuH_2(CO)(PPh_3)_3$ -Catalyzed Regioselective Arylation of Aromatic Ketones with Arylboronates via Carbon−Hydrogen Bond Cleavage. *J. Am. Chem. Soc.* **2005**, *127*, 5936–5945. (c) Kitazawa, K.; Kochi, T.; Sato, M.; Kakiuchi, F. Convenient Synthesis of Tetra- And Hexaarylanthracenes by Means of $RuH_2(CO)(PPh_3)_3$-Catalyzed C–H Arylation of Anthraquinone with Arylboronates. *Org. Lett.* **2009**, *11*, 1951–1954. (d) Kitazawa, K.; Kotani, M.; Kochi, T.; Langeloth, M.: Kakiuchi, F. $RuH_2(CO)(PPh_3)_3$-Catalyzed Arylation of Aromatic Esters Using Arylboronates via C–H Bond Cleavages. *J. Organomet. Chem.* **2010**, *695*, 1163–1167. (e) Kitazawa, K.; Kochi, T.; Nitani, M.; Ie, Y.; Aso, Y.; Kakiuchi, F. Convenient Synthesis of Dibenzo[a,h]Anthracenes and Picenes via C–H Arylation of Acetophenones with

Arenediboronates. *Chem*. *Lett*. **2011**, *40*, 300–302. (f) Ogiwara, Y.; Miyake, M.; Kochi, T.; Kakiuchi, F. Syntheses of $RuHCl(CO)(PAr_3)_3$ and $RuH_2(CO)(PAr_3)_3$ Containing Various Triarylphosphines and Their Use for Arylation of Sterically Congested Aromatic C–H Bonds. *Organometallics* **2017**, *36*, 159–164. See also ref 3b.

(6) C–O functionalization: (a) Kakiuchi, F.; Usui, M.; Ueno, S.; Chatani, N.; Murai, S. Ruthenium-Catalyzed Functionalization of Aryl Carbon–Oxygen Bonds in Aromatic Ethers with Organoboron Compounds. *J*. *Am*. *Chem*. *Soc*. **2004**, *126*, 2706–2707. (b) Ueno, S.; Mizushima, E.; Chatani, N.; Kakiuchi, F. Direct Observation of the Oxidative Addition of the Aryl Carbon−Oxygen Bond to a Ruthenium Complex and Consideration of the Relative Reactivity between Aryl Carbon−Oxygen and Aryl Carbon−Hydrogen Bonds. *J*. *Am*. *Chem*. *Soc*. **2006**, *128*, 16516–16517. (c) Kondo, H.; Akiba, N.; Kochi, T.; Kakiuchi, F. Ruthenium-Catalyzed Monoalkenylation of Aromatic Ketones by Cleavage of Carbon–Heteroatom Bonds with Unconventional Chemoselectivity. *Angew*. *Chem*., *Int*. *Ed*. **2015**, *54*, 9293–9297. (d) Kondo, H.; Kochi, T.; Kakiuchi, F. Selective Monoarylation of Aromatic Ketones and Esters via Cleavage of Aromatic Carbon–Heteroatom Bonds by Trialkylphosphine Ruthenium Catalysts. *Org. Lett.* **2017**, *19*, 794–797.

(7) C–N and C–F functionalizations: (a) Ueno, S.; Chatani, N.; Kakiuchi, F. Ruthenium-Catalyzed Carbon–Carbon Bond Formation via the Cleavage of an Unreactive Aryl Carbon–Nitrogen Bond in Aniline Derivatives with Organoboronates. *J*. *Am*. *Chem*. *Soc*. **2007**, *129*, 6098–6099. (b) Koreeda, T.; Kochi, T.; Kakiuchi, F. Cleavage of C−N Bonds in Aniline Derivatives on a Ruthenium Center and Its Relevance to Catalytic C−C Bond Formation. *J*. *Am*. *Chem*. *Soc*. **2009**, *131*, 7238–7239. (c) Koreeda, T.; Kochi, T.; Kakiuchi, F. Substituent Effects on Stoichiometric and Catalytic Cleavage of Carbon–Nitrogen Bonds in Aniline Derivatives by

Ruthenium-Phosphine Complexes. *Organometallics* **2013**, *32*, 682–690. (d) Koreeda, T.; Kochi, T.; Kakiuchi, F. Ruthenium-Catalyzed Reductive Deamination and Tandem Alkylation of Aniline Derivatives. *J. Organomet. Chem.* **2013**, *741-742*, 148–152. (e) Kawamoto, K.; Kochi, T.; Sato, M.; Mizushima, E.; Kakiuchi, F. Ruthenium-Catalyzed Arylation of Fluorinated Aromatic Ketones via Ortho-Selective Carbon–Fluorine Bond Cleavage. *Tetrahedron Lett.* **2011**, *52*, 5888-5890. See also ref 6c and 6d.

(8) Koseki, Y.; Kitazawa, K.; Miyake, M.; Kochi, T.; Kakiuchi, F. Ruthenium-Catalyzed Ortho C–H Arylation of Aromatic Nitriles with Arylboronates and Observation of Partial Para Arylation. *J. Org. Chem.* **2017**, *82*, 6503-6510.

(9) Andersen, T. L.; Frederiksen, M. W.; Domino, K.; Skrydstrup, T. Direct Access to *α,α*-Difluoroacylated Arenes by Palladium-Catalyzed Carbonylation of (Hetero)Aryl Boronic Acid Derivatives. *Angew. Chem., Int. Ed.* **2016**, *55*, 10396–10400.

(10) (a) Ronson, T. O.; Renders, E.; Van Steijvoort, B. F.; Wang, X.; Wybon, C. C. D.; Prokopcová, H.; Meerpoel, L.; Maes, B. U. W. Ruthenium-Catalyzed Reductive Arylation of *N*-(2-Pyridinyl)Amides with Isopropanol and Arylboronate Esters. *Angew. Chem. Int. Ed.* **2019**, *58*, 482–487. (b) Takaya, J.; Tadami, S.; Ukai, K.; Iwasawa, N. Copper(I)-Catalyzed Carboxylation of Aryl- and Alkenylboronic Esters. *Org. Lett.* **2008**, *10*, 2697-2700.

(11) Esteruelas, M. A.; Werner, H. Five- and Six-Coordinate Hydrido(Carbonyl)-Ruthenium(II) and -Osmium(II) Complexes Containing Triisopropylphosphine as Ligand. *J. Organomet. Chem.* **1986**, *303*, 221–231.

(12) Huang, D.; Folting, K.; Caulton, K. G. Reactivity of $RuCl_2(CO)(P^tBu_2Me)_2$ toward H_2 and Brønsted Acids: Aggregation Triggered by Protonation and Phosphine Loss. *Inorg. Chem.* **1996**, *35*, 7035–7040.

(13) Martin, P.; McManus, N. T.; Rempel, G. L. Detailed Study of the Hydrogenation of Nitrile-Butadiene Rubber and Other Substrates Catalyzed by Ru(II) Complexes. *J. Mol. Catal. A: Chem.* **1997**, *126*, 115–131.

(14) Korn, T. J.; Schade, M. A.; Cheemala, M. N.; Wirth, S.; Guevara, S. A.; Cahiez, G.; Knochel, P. Cobalt-Catalyzed Cross-Coupling Reactions of Heterocyclic Chlorides with Arylmagnesium Halides and of Polyfunctionalized Arylcopper Reagents with Aryl Bromides, Chlorides, Fluorides and Tosylates. *Synthesis* **2006**, *2006*, 3547–3574.

(15) Ackermann, L. Phosphine Oxides as Preligands in Ruthenium-Catalyzed Arylations via C–H Bond Functionalization Using Aryl Chlorides. *Org. Lett*. **2005**, *7*, 3123–3125.

(16) Goossen, L. J.; Rodríguez, N.; Linder, C. Decarboxylative Biaryl Synthesis from Aromatic Carboxylates and Aryl Triflates. *J. Am. Chem. Soc.* **2008**, *130*, 15248-15249.

(17) McBurney, R. T.; Slawin, A. M. Z.; Smart, L. A.; Yu, Y.; Walton, J. C. UV Promoted Phenanthridine Syntheses from Oxime Carbonate Derived Iminyl Radicals. *Chem. Commun.* **2011**, *47*, 7974-7976.

(18) Pan, F.; Wang, H.; Shen, P.-X.; Zhao, J.; Shi, Z.-J. Cross Coupling of Thioethers with Aryl Boroxines to Construct Biaryls via Rh Catalyzed C–S Activation. *Chem. Sci.* **2013**, *4*, 1573-1577.

(19) Motti, E.; Della Ca', N.; Xu, D.; Piersimoni, A.; Bedogni, E.; Zhou, Z.-M.; Catellani, M. A Sequential Pd/Norbornene-Catalyzed Process Generates *o*-Biaryl Carbaldehydes or Ketones via a Redox Reaction or 6*H*-Dibenzopyrans by C–O Ring Closure. *Org. Lett.* **2012**, *14*, 5792-5795.

(20) Yoshikai, N.; Matsumoto, A.; Norinder, J.; Nakamura, E. Iron-Catalyzed Chemoselective *ortho* Arylation of Aryl Imines by Directed C–H Bond Activation. *Angew. Chem., Int. Ed.* **2009**, *48*, 2925-2928.

(21) Arisawa, M.; Suwa, K.; Yamaguchi, M. Rhodium-Catalyzed Methylthio Transfer Reaction between Ketone α-Positions: Reversible Single-Bond Metathesis of C−S and C−H Bonds. *Org. Lett.* **2009**, *11*, 625-627.

(22) Yoshikai, N.; Matsumoto, A.; Norindar, J.; Nakamura, E. Iron-Catalyzed Direct Arylation of Aryl Pyridines and Imines Using Oxygen as an Oxidant. *Synlett* **2010**, *2010*, 313–316.