Supporting Information For:
**Iron-Catalyzed Cross-Coupling of Primary and Secondary Alkyl Halides with Aryl
Grignard Reagents**

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General. All the reactions dealing with air or moisture sensitive compounds were carried out in a dry reaction vessel under a positive pressure of argon or nitrogen. Air- and moisture-sensitive liquids and solutions were transferred via syringe or stainless steel cannula. Analytical thin-layer chromatography was performed using glass plates pre-coated with 0.25-mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light (UV) and/or by immersion in an acidic staining solution of *p*-anisaldehyde followed by heating on a hot plate. Organic solutions were concentrated by rotary evaporation at ~15 Torr (evacuated with a diaphragm pump). Flash column chromatography was performed as described by Still et al.,¹ employing Kanto Silica gel 60 (spherical, neutral, 140-325 mesh).

Materials. Commercial reagents were purchased from Tokyo Kasei Co., Aldrich Inc., and other commercial suppliers and were used either distilled or recrystallized before use. Anhydrous tetrahydrofuran (THF) was purchased from Kanto Chemical Co. and distilled from benzophenone ketyl at 760 Torr under an argon atmosphere immediately before use. The water content of the solvent was confirmed with a Karl-Fischer moisture titrator to be less than 20 ppm. FeCl₃ purchased from Kanto Chemical Co., was dehydrated by SOCl₂, and dried thoroughly under reduced pressure, and the resulting anhydrous FeCl₃ was stored under argon. A 0.1-M THF solution of FeCl₃ tends to form polyether compounds upon room-temperature storage for days, and thus, was prepared immediately before use.

(1) Still, W. C.; Klahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2924.

Instrumentation. Proton nuclear magnetic resonance (^1H NMR) and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded with JEOL AL-400 (400 MHz), JEOL ECX-400 (400 MHz) or JEOL ECA-500 (500 MHz) NMR spectrometers. Chemical shifts for protons are reported in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent (CDCl_3 : δ 7.26). Carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded at 125 or 100 MHz: chemical shifts for carbons are reported in parts per million (ppm, δ scale) downfield from tetramethylsilane and are referenced to the carbon resonance of the solvent (CDCl_3 : δ 77.0). Data is presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and/or multiplet resonances, br = broad), coupling constant in Hertz (Hz), and integration. Gas chromatographic (GC) analyses were performed on Shimadzu GC-14B instruments equipped with an FID detector and a capillary column, HR-1 (25 m $\times$ 0.25 mm i.d., 0.25 μm film) or a CYCLOSILB (Agilent, 30 m $\times$ 0.25 mm i.d., 0.25 μm film) or a CHIRALDEX G-TA (ASTEC, 20 m $\times$ 0.25 mm i.d., 0.125 μm film). IR spectra recorded on a React IR 1000 Reaction Analysis System equipped with DuraSample IR (ASI Applied System) are reported in cm^{-1} . Mass spectra are taken at JEOL GC-mate II.

Studies on the effect of additives on the product selectivity and yield, and screening of catalyst precursor.

A typical procedure for the cross coupling reaction in Table S1: A 50-mL glass tube containing a magnetic stirring bar, a 0.96-M THF solution of phenylmagnesium bromide (1.25 mL, 1.2 mmol), an additive (1.2 mmol) and bromocycloheptane (137 μL , 1.0 mmol) was cooled to -78°C . A 0.1-M THF solution of FeCl_3 (0.5 mL, 5 mol%) was added at that temperature. The resulting solution was immersed to an ice-water bath and stirred for 30 min at 0°C . A saturated aqueous solution of NH_4Cl (0.5 mL) was added to quench the reaction. After a standard aqueous work up, total consumption of **1**, and the yields of **2**, **3**, **4** and biphenyl were determined by Gas chromatographic analysis (GC) using an internal standard (n-decane, 98 μL , 0.5 mmol).

Effect of the additives: Investigation of other additives was carried out according to the experimental procedure described above and the results are summarized in Table S1.

Table S1. The effect of additives on the product selectivity and yield.

entry	additive	% yield ^a				
		2	3	4	1	Ph-Ph
1	none	5	79	0	4	6
2	Et ₃ N (1.2 equiv)	3	78	0	11	5
3	<i>N</i> -methyl morpholine (1.2 equiv)	8	72	0	4	5
4	DABCO (1.2 equiv)	20	2	0	75	3
5	TMEDA (1.2 equiv)	71	19	3	trace	10
6	Et ₂ N-CH ₂ -CH ₂ -NEt ₂ (1.2 equiv)	23	48	1	11	9
7	NMP (1.2 equiv)	15	3	trace	79	4
8	PPh ₃ (0.1 equiv)	6	70	trace	6	7
9	dppe (0.05 equiv)	4	8	0	81	8

^aThe reaction conditions are described above. The yield was determined by GC with decane as an internal standard.

Cross-coupling reactions with different catalyst precursors: Screening of some iron compounds as a catalyst precursor was carried out according to a similar procedure described above and the results are summarized in Table S2.

Table S2. The iron-catalyzed coupling reaction with different catalyst precursors

entry	cat. Fe	% yield ^a				
		2	3	4	1	Ph-Ph
1	FeCl ₃	71	19	3	trace	10
2	FeF ₃	0	0	0	97	2
3	Fe(acac) ₃	14	6	1	71	10
4	FeCl ₂	32	10	1	56	10
5	Fe(CO) ₅	trace	trace	0	95	5

^aThe reaction conditions are described above. The yield was determined by GC with decane as an internal standard.

Iron-catalyzed cross-coupling reactions of an alkyl halide and a Grignard reagent.

Scope and limitations of the present coupling reactions were studied according to the procedures described below and the results are summarized in Table S3.

Table S3. Iron-catalyzed coupling reaction of an alkyl halide with an aryl Grignard reagent.^a

entry ^b	alkyl halide	ArMgBr	product	% yield ^{c,d}	
1		Ar = Ph		96 (90) ^{e,f}	
2		Ar = Ph		99 (X = I)	
3				99 (X = Br) ^e	
4				99 (X = Cl) ^g	
5		Ar = 4-MeOC ₆ H ₄		99 ^e	
6		Ar = 4-MeC ₆ H ₄		96 ^e	
7		Ar = 4-CF ₃ C ₆ H ₄		67 ^{e,h}	
8 ⁱ		Ar = 2-naphtyl		96	
9 ^j		Ar = 1-naphtyl		97 ^j	
10		Ar = 2-MeC ₆ H ₄		98 ^e	
11		Ar = Ph		95 (X = I)	
12				94 (X = Br)	
13				84 (X = Cl) ^{g,k}	
14	<i>n</i> -C ₈ H ₁₇ -X	Ar = Ph	<i>n</i> -C ₈ H ₁₇ -Ph	97 (X = I)	
15				91 (X = Br)	
16				45 (X = Cl) ^{g,k}	
17		Ar = 4-MeOC ₆ H ₄	(<i>exo:endo</i> = 95:5)	91	
18 ^l		Ar = 4-MeOC ₆ H ₄	(<i>trans:cis</i> = 96:4)	96 ^e	
19 ^l		Ar = 4-MeOC ₆ H ₄	(<i>trans:cis</i> = 96:4)	98	
20		Ar = 4-MeOC ₆ H ₄		88 ^e	
21		Ar = 4-MeOC ₆ H ₄		87 ^e	

^aThe reaction was carried out on a 1-mmol scale under the slow addition conditions unless otherwise noted. ^bReaction temperature was 0 °C in entries 1–3, 11, 14 and 17–21, and 25 °C in entries 4–10, 12 and 15 unless otherwise noted. ^c1.2 equiv of Grignard reagent was used unless otherwise noted. ^dThe yield refers to the one determined by GC with an internal standard unless otherwise noted. ^eIsolated yield. ^fThe large scale experiment in the text. ^g1.5 equiv of Grignard reagent was used. ^h2.0 equiv of Grignard reagent was used. ⁱGrignard reagent was added to a mixture of bromocyclohexane, FeCl₃, and TMEDA. ^j1.8 equiv of Grignard reagent was used. ^kThe reaction temperature was 40 °C. ^l0.5-mmol scale.

A procedure for the cross-coupling reaction of bromocycloheptane and phenylmagnesium bromide (PhMgBr) on 50-mmol scale.

Cycloheptylbenzene: To a mixture of bromocycloheptane (8.85 g, 50 mmol), FeCl₃ (25 mL of a 0.1-M THF solution, 5 mol%) was added at 0 °C a mixture of PhMgBr (72 mL of a 0.93-M THF solution, 67 mmol) and TMEDA (7.78 g, 67 mmol) via syringe pump with such a rate that keeps the reaction mixture a pale yellow solution (1.36 mL/min in this case). The reaction mixture was stirred at that temperature for 10 min after completion of the addition of PhMgBr/TMEDA. After aqueous workup, distillation of the product mixture afforded phenylcycloheptane as a colorless oil (8.18 g containing 0.37 g of biphenyl, 90% yield); FTIR (neat): cm⁻¹ 3062, 3027, 2923 (s), 2854 (s), 1602, 1492, 1461, 1451, 1073, 1032, 753 (m), 737 (m), 698 (m); ¹H NMR (500 MHz, CDCl₃): δ 7.28–7.24 (m, 2H), 7.19–7.12 (m, 3H), 2.68–2.63 (m, 1H), 1.93–1.90 (m, 2H), 1.81–1.78 (m, 2H), 1.67–1.51 (m, 8H); ¹³C NMR (125 MHz, CDCl₃): δ 150.0, 128.2 (2C), 126.6 (2C), 125.5, 47.1, 36.8 (2C), 27.9 (2C), 27.2 (2C); HRMS (EI, 70 eV) *m/z* [M]⁺ calcd for C₁₃H₁₈, 174.1409; found, 174.1418.

A typical procedure for the cross-coupling reactions except entries 9 and 10 in Table S3.

Cyclohexylbenzene: To a mixture of bromocyclohexane (163.1 mg, 1.0 mmol), FeCl₃ (500 μL of a 0.1-M THF solution, 5 mol%) was added a mixture of phenylmagnesium bromide (1.25 mL of a 0.96-M THF solution, 1.2 mmol) and TMEDA (181.1 μL, 1.2 mmol) via syringe pump for 20 min at 0 °C. The reaction mixture was stirred at that temperature for 10 min after completion of the addition of the mixture of the Grignard reagent and TMEDA. After aqueous workup, the reaction mixture was filtered through a pad of Florisil[®], and concentrated *in vacuo*. ¹H NMR analysis of the crude product showed, upon comparison with the integration of an internal standard (tetrachloroethane, 79 mg, 0.47 mmol), that cyclohexylbenzene was obtained in 99% yield. Analysis by GC also showed that the yield of cyclohexylbenzene was 99%. Analytical data for cyclohexylbenzene have been previously reported.²

1-Cyclohexyl-4-methoxybenzene: The titled compound was obtained in 99 % yield by ¹H NMR analysis upon comparison with the integration of an internal standard (tetrachloroethane,

(2) Singh, R. P.; Kamble, R. M.; Chandra, K. L.; Saravanan, C. P.; Siingh, V. K. *Tetrahedron* **2001**, 57, 241–247.

79 mg, 0.47 mmol). Purification with silica gel chromatography afforded the desired product as a pale yellow solid (190 mg, 99 % yield); FTIR (neat): cm^{-1} 2919 (s), 2850 (m), 1513 (s), 1449 (m), 1248 (s), 1177 (s), 1032 (s), 814 (s); ^1H NMR (500 MHz, CDCl_3): δ 7.12 (d, J = 8.5 Hz, 2H), 6.83 (d, J = 8.5 Hz, 2H), 3.78 (s, 3H), 2.50–2.38 (m, 1H), 1.92–1.79 (m, 4H), 1.78–1.65 (m, 1H), 1.45–1.30 (m, 4H), 1.28–1.15 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 157.6, 140.3, 127.6 (2C), 113.6 (2C), 55.2, 43.6, 34.7 (2C), 26.9 (2C), 26.1; HRMS (EI, 70 eV) m/z $[\text{M}]^+$ calcd for $\text{C}_{13}\text{H}_{18}\text{O}$, 190.1358; found, 190.1381; Anal. Calcd for $\text{C}_{13}\text{H}_{18}\text{O}$: C, 82.06; H, 9.53. Found: C, 81.80; H, 9.80. All analytical data are in good accordance with those reported in the literature.²

1-Cyclohexyl-4-methylbenzene: The titled compound was obtained in 98 % yield by ^1H NMR analysis upon comparison with the integration of an internal standard (tetrachloroethane, 79 mg, 0.47 mmol). Purification with silica gel chromatography afforded the desired product as a colorless oil (167 mg, 96% yield); FTIR (neat): cm^{-1} 2923 (s), 2852 (m), 1515 (m), 1447 (m), 809 (s); ^1H NMR (500 MHz, CDCl_3): δ 7.10 (s, 4H), 2.50–2.40 (m, 1H), 2.30 (s, 3H), 1.90–1.79 (m, 4H), 1.78–1.67 (m, 1H), 1.45–1.32 (m, 4H), 1.29–1.17 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 146.0, 136.0, 129.7 (2C), 127.4 (2C), 44.4, 34.8 (2C), 27.1 (2C), 26.3, 21.1; HRMS (EI, 70 eV) m/z $[\text{M}]^+$ calcd for $\text{C}_{13}\text{H}_{18}$, 147.1409; found, 147.1388; Anal. Calcd for $\text{C}_{13}\text{H}_{18}$: C, 89.59; H, 10.41. Found: C, 89.34; H, 10.64. All analytical data are in good accordance with those reported in the literature.³

1-Cyclohexyl-4-trifluoromethylbenzene: The titled compound was obtained in 70 % yield by ^1H NMR analysis upon comparison with the integration of an internal standard (tetrachloroethane, 79 mg, 0.47 mmol). Purification with silica gel chromatography afforded the coupling product as a colorless oil (153 mg, 67% yield); FTIR (neat): cm^{-1} 2927 (m), 2856, 1619, 1451, 1420, 1324 (s), 1162, 1119 (s), 1069 (s), 1017, 830 (s), 656; ^1H NMR (500 MHz, CDCl_3): δ 7.53 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 2.61–2.51 (m, 1H), 1.94–1.74 (m, 5H), 1.48–1.34 (m, 4H), 1.33–1.19 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3): δ 152.1, 128.2 (q, J = 32.4 Hz), 127.2 (2C), 124.5 (q, J = 270.8 Hz), 125.2 (q, J = 3.8 Hz, 2C), 44.5, 34.2 (2C), 26.7 (2C), 26.0; HRMS (EI, 70 eV) m/z $[\text{M}]^+$ calcd for $\text{C}_{13}\text{H}_{15}\text{F}_3$, 228.1126; found 228.1144; Anal. Calcd for $\text{C}_{13}\text{H}_{15}\text{F}_3$: C, 68.41; H, 6.62. Found: C, 68.49; H, 6.83.

An alternative procedure for the cross-coupling reactions (entries 9 and 10 in Table S3).

2-Cyclohexylnaphthalene: To a mixture of bromocyclohexane (163.1 mg, 1.0 mmol), FeCl₃ (500 μ L of a 0.1 M-THF solution, 5 mol%) and TMEDA (181.1 μ L, 1.2 mmol) was added 2-naphthylmagnesium bromide (1.46 mL of a 0.82 M-THF solution, 1.2 mmol) via syringe pump for 20 min at 25 °C. The reaction mixture was stirred at that temperature for 10 min after completion of the addition of the mixture of the Grignard reagent. After aqueous workup, the reaction mixture was filtered through a pad of Florisil[®], and concentrated *in vacuo*. ¹H NMR analysis of the crude product with an internal standard (tetrachloroethane, 79mg, 0.47 mmol) showed that the 2-cyclohexylnaphthalene was obtained in 96% yield. Analytical data for the compound have been previously reported.³

1-Cyclohexylnaphthalene: The titled compound was obtained in 97 % yield by ¹H NMR analysis upon comparison with the integration of an internal standard (tetrachloroethane, 79 mg, 0.47 mmol); ¹H NMR (500 MHz, CDCl₃): δ 8.11 (br d, J = 8.3 Hz, 1H), 7.84–7.81 (m, 1H), 7.67 (br d, J = 8.3 Hz, 1H), 7.50–7.36 (m, 4H), 3.35–3.27 (m, 1H), 2.06–1.98 (m, 2H), 1.95–1.86 (m, 2H), 1.86–1.80 (m, 1H), 1.58–1.50 (m, 4H), 1.38–1.27 (m, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 143.7, 133.9, 131.3, 128.9, 126.2, 125.6, 125.5, 125.2, 123.2, 122.2, 39.2, 34.15 (2C), 27.2 (2C), 26.5; HRMS (EI, 70 eV) m/z [M]⁺ calcd for C₁₆H₁₈, 210.1409; found, 210.1433.

1-Cyclohexyl-2-methylbenzene: The titled compound was obtained in 99 % yield by ¹H NMR analysis upon comparison with the integration of an internal standard (tetrachloroethane, 79 mg, 0.47 mmol). Purification with silica gel chromatography afforded the desired product as a colorless oil (171 mg, 98% yield); FTIR (neat): cm⁻¹ 3064, 3022, 2925 (s), 2852 (m), 1492, 1448 (m), 741 (s), 723 (s); ¹H NMR (500 MHz, CDCl₃): δ 7.22–7.05 (m, 4H), 2.75–2.63 (m, 1H), 2.33 (s, 3H), 1.91–1.73 (m, 5H), 1.47–1.34 (m, 4H), 1.33–1.23 (m, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 145.9, 135.1, 130.1, 126.1, 125.4, 125.3, 40.0, 33.6 (2C), 27.1 (2C), 26.3, 19.3; HRMS (EI, 70 eV) m/z [M]⁺ calcd for C₁₃H₁₈, 147.1409; found, 147.1427. Anal. Calcd for C₁₃H₁₈: C, 89.59; H, 10.41. Found: C, 89.56; H, 10.69. All analytical data are in good accordance with those reported in the literature.²

(3) Yonehara, F.; Kido, Y.; Sugimoto, H.; Morita, S.; Yamaguchi, M. *J. Org. Chem.* **2001**, 68, 241–247.

Analytical data of **2-butylbenzene**⁴ and **2-octylbenzene**⁵ have been reported in the literature.

1-(*exo*-2-Norbornyl)-4-methoxybenzene: The titled compound was obtained in 91 % yield by ¹H NMR analysis upon comparison with the integration of an internal standard (tetrachloroethane, 79 mg, 0.47 mmol); The diastereomeric composition of the product was determined as 95:5 by capillary GC analysis (CHIRALDEX G-TA, ASTEC, 20 m × 0.25 mm, 0.125 μm film, 140 °C), where the peaks corresponding to *exo*- and *end*- isomers were appeared at the retention times of 27.9 and 30.4 min, respectively. Analytical data of the compound have been reported in the literature.⁶

1-(4-*tert*-Butylcyclohexyl)-4-methoxybenzene: The titled compound was obtained as a white solid (118.6 mg, 96% yield). Capillary GC analysis (CHIRALDEX G-TA, ASTEC, 20 m × 0.25 mm, 0.125 μm film, 150 °C) showed a 96:4 ratio of *trans*- and *cis*- isomers (retention times; 67.4 and 56.2 min, respectively). FTIR (neat): cm⁻¹ 2925 (s), 2854 (s), 1611, 1582, 1513 (s), 1486, 1465, 1451, 1393, 1366, 1248 (s), 1181 (m), 1038 (s), 1034 (s), 824 (m), 801 (m); ¹H NMR (400 MHz, CDCl₃): δ 7.12 (d, *J* = 8.8 Hz, 2H), 6.83 (d, *J* = 8.8 Hz, 2H), 3.78 (s, 3H), 2.42–2.35 (m, 1H), 1.93–1.86 (m, 4H), 1.43–1.35 (m, 2H), 1.18–1.03 (m, 3H), 0.83 (s, 9H); ¹³C NMR (100 MHz, CDCl₃): δ 157.7, 140.1, 127.7 (2C), 113.7 (2C), 55.2, 47.7, 35.02, 34.4 (2C), 32.6, 27.7 (2C), 27.6 (3C); HRMS (EI, 70 eV) *m/z* [M]⁺ calcd for C₁₇H₂₆O₁ 246.1984; found 246.1985.

2-Octylbenzene prepared from optically active (*S*)-2-bromooctane: The titled compound was obtained as a colorless oil (84.0 mg 88% yield) after silica gel column chromatography. Analytical data of the titled compound have been reported in the literature.⁷ The enantiomeric excess of the compound was determined as 0 % ee by capillary GC analysis (CYCLOSILB, Agilent, 30 m × 0.25 mm i.d., 0.25 μm film, 80 °C for 120 min and increment of the oven temperature by the rate of 1 °C/min). Peaks at the retention times of 125.2 and 129.1, which correspond to the enantiomers, were observed in a 50:50 ratio.

Ethyl 6-(*p*-methoxyphenyl)hexanoate: The titled compound was obtained in 91 % yield by ¹H NMR analysis upon comparison with the integration of an internal standard (tetrachloroethane,

(4) Tramontini, M; Angiolini, L. *Tetrahedron* **1973**, *29*, 4183–4187.

(5) Hall, S. S.; McEnroe, F. J. *J. Org. Chem.*, **1975**, *40*, 271–275.

99 mg, 0.57 mmol). Purification of with silica gel chromatography afforded the desired product as colorless liquid (220 mg, 88 % yield). Analytical data of the compound is reported in the literature. ⁷

***N*-[3-(4-Methoxyphenyl)propyl]indole:** The titled compound was obtained in 93 % yield by ¹H NMR analysis upon comparison with the integration of an internal standard (dibromomethane, 99 mg, 0.57 mmol). Purification with silica gel chromatography afforded the desired product as a colorless oil (231 mg, 87% yield); ¹H NMR (500 MHz, CDCl₃): δ 7.63 (d, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.19 (t, *J* = 8.0 Hz, 1H), 7.12–7.06 (m, 4H), 6.83 (d, *J* = 8.5 Hz, 1H), 6.49 (d, *J* = 3.5 Hz, 1H), 4.10 (t, *J* = 7.0 Hz, 2H), 3.79 (s, 3H), 2.57 (t, *J* = 7.5 Hz, 2H), 2.15 (distorted tt, *J* = 7.5, 7.0 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃): δ 157.9, 135.9, 132.9, 129.3, 128.5, 127.8, 127.7, 121.3, 120.9, 119.1, 114.1, 113.8, 109.3, 100.96, 55.2, 45.5, 32.0, 31.6; HRMS (EI, 70 eV) *m/z* [M]⁺ calcd for C₁₈H₁₉N₁O₁ 265.1467; found 265.1478; Anal. Calcd for C₁₈H₁₉NO: C, 81.48; H, 7.22; N, 5.28. Found: C, 81.38; H, 7.49; N, 5.23.

(6) Wu, X.-Y.; Xu, H.-D.; Tang, F.-Y.; Zhou, Q.-L. *Tetrahedron: Asymmetry* **2001**, *12*, 2565–2567.

(7) Lee, J.-Y.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 5616–5617.