## Iron-Catalyzed Grignard Cross-Coupling Reaction with Alkyl Halides Possessing $\beta\text{-Hydrogens}$

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## **Supporting Data**

**General.** All anaerobic and/or moisture sensitive manipulations were carried out with standard Schlenk techniques under predried nitrogen or with glovebox techniques under prepurified argon. Tetrahydrofuran and diethyl ether were distilled from sodium benzophenone-ketyl under nitrogen prior to use. NMP, 1-bromooctane (**2n**), 1-chlorooctane, 1-iodooctane, 1-bromo-4-phenoxybutane (**2o**), and bromocyclohexane (**2q**) were obtained from commercial suppliers and used without further purification. Tris(acetylacetonato)-iron(III)<sup>1</sup>, *n*-octyl tosylate<sup>2</sup>, 2-bromooctane (**2p**)<sup>3</sup>, and 1-bromo-5-phenylpentane (**2m**)<sup>4</sup> were prepared according to the literature methods. NMR spectra were recorded on a JEOL JNM LA500 spectrometer (<sup>1</sup>H, 500 MHz; <sup>13</sup>C, 125 MHz). <sup>1</sup>H and <sup>13</sup>C chemical shifts are reported in ppm downfield of internal tetramethylsilane.

## Synthesis of 1-bromo-3-(4-trifluoromethanesulfonyloxyphenyl)propane (7). To a



mixture of 4-(3-bromopropyl)phenol<sup>5</sup> (1.53 g, 7.1 mmol) and pyridine (0.97 mL, 12 mmol) in  $CH_2Cl_2(15 mL)$  was added dropwise  $Tf_2O$  (1.55 mL, 9.2 mmol) at 0 °C, and the mixture was stirred at room temperature for 1 h. The resulting mixture was concentrated under reduced pressure and the residue was

dissolved in benzene. The benzene solution was washed with 1 N HCl, saturated NaHCO<sub>3</sub> and brine, and dried over anhydrous magnesium sulfate. The solvent was removed and the residue was chromatographed on silica gel (pentane/diethyl ether = 4:1) to give **7** (2.47 g, 7.1 mmol). Yield: 100%. <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  2.14-2.19 (m, 2H), 2.82 (t, *J* = 7.5 Hz, 2H), 3.39 (t, *J* = 6.4 Hz, 2H), 7.20 (d, *J* = 8.7 Hz, 2H), 7.28 (d, *J* = 8.7 Hz, 2H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>):  $\delta$  32.56, 33.25, 33.76, 118.74 (q, *J*<sub>C-F</sub> = 320.0 Hz), 121.34, 130.26, 141.16, 148.01. Anal. Calcd for C<sub>10</sub>H<sub>10</sub>O<sub>3</sub>F<sub>3</sub>SBr: C, 34.60; H, 2.90. Found: C, 34.80; H, 2.92.

**Iron-Catalyzed Cross-Coupling Reaction.** A mixture of 1-bromooctane (100 mg, 0.52 mmol) and Fe(acac)<sub>3</sub> (9.0 mg, 0.026 mmol) in Et<sub>2</sub>O (3 mL) was warmed to reflux. To this was added *p*-tolylmagnesium bromide (1.67 M in Et<sub>2</sub>O, 0.70 mL, 1.04 mmol), resulting in an immediate color change from red to black. The mixture was refluxed for 30 minutes and then poured into aqueous HCl solution (1 N). It was extracted with Et<sub>2</sub>O, and the extracts were dried over anhydrous magnesium sulfate. The solvent was removed and the residue was chromatographed on silica gel to give 1-(*p*-tolyl)octane (**3an**) (74.0 mg, 0.36 mmol). Yield: 70%. Registry No. of the known compounds are as follows: **3an**, 7686-25-1; **3bn**, 3307-19-5; **3cn**, 28593-20-6; **3dn**, 79835-99-7; **3am**, 38425-25-1; **3ap**, 90734-22-8; **3aq**, 4501-36-4; **3en**, 177969-49-2; **4**, 1075-74-7; **5**, 538-68-1; **6**, 613-33-2. The characterization data of the new compounds are described below.

**4-(4-phenoxybutyl)toluene (3ao).** <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 1.74-1.84 (m, 4H), 2.31 (s,



3H), 2.64 (t, J = 7.3 Hz, 2H), 3.95 (t, J = 6.0 Hz, 2H), 6.87 (d, J = 8.3 Hz, 2H), 6.90-6.93 (m, 1H), 7.08 (singlet-like m, 4H), 7.24-7.28 (m, 2H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>):  $\delta$  20.96, 27.94, 28.87, 35.12, 67.64, 114.49, 120.48, 128.28, 128.98, 129.38, 135.16, 139.12, 159.07. Anal. Calcd for

C<sub>17</sub>H<sub>20</sub>O: C, 84.96; H, 8.39. Found: C, 85.13; H, 8.39.



1-(4-tolyl)-3-(4-trifluoromethanesulfonyloxyphenyl)propane (8). <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  1.90-1.96 (m, 2H), 2.32 (s, 3H), 2.60 (t, J = 7.6 Hz, 2H), 2.65 (t, J = 7.8 Hz, 2H), 7.06 (d, J = 8.1 Hz, 2H), 7.09 (d, J = 8.1 Hz, 2H), 7.16 (d, J = 8.6 Hz, 2H), 7.23 (d, J = 8.6 Hz, 2H). <sup>13</sup>C{<sup>1</sup>H} NMR (CDCl<sub>3</sub>):  $\delta$  20.96, 32.77, 34.67, 34.83, 118.76 (q, *J*<sub>C-F</sub> = 320.6 Hz), 121.05, 128.26,

129.06, 130.06, 135.36, 138.64, 142.94, 147.73. Anal. Calcd for C<sub>17</sub>H<sub>17</sub>O<sub>3</sub>F<sub>3</sub>S: C, 56.97; H, 4.78. Found: C, 57.24; H, 4.82.

**1-(4-tolyl)-3-(4-***n***-butylphenyl)propane (9).** <sup>1</sup>H NMR (CDCl<sub>3</sub>):  $\delta$  0.92 (t, J = 7.3 Hz,



3H), 1.31-1.38 (m, 2H), 1.55-1.61 (m, 2H), 1.89-1.95 (m, 2H), 2.31 (s, 3H), 2.55-2.62 (m, 6H), 7.07-7.08 (m, 8H).  ${}^{13}C{}^{1}H{}$  NMR (CDCl<sub>3</sub>):  $\delta$  13.95, 20.98, 22.39, 33.06, 33.72, 35.01, 35.24, 128.26, 128.29, 128.30, 128.95, 135.07, 139.28, 139.46, 140.18.

Anal. Calcd for C<sub>20</sub>H<sub>26</sub>: C, 90.16; H, 9.84. Found: C, 90.41; H, 9.88.

Determination of the amount of initially formed 4,4'-bitolyl in the reduction of  $Fe(acac)_3$ . To a solution of  $Fe(acac)_3$  (90.0 mg, 0.255 mmol) in Et<sub>2</sub>O (30 mL) was added ptolylmagnesium bromide (1.67 M in Et<sub>2</sub>O, 6.0 mL, 3.59 mmol) at 0 °C. The mixture was stirred for 30 minutes and then poured into aqueous HCl solution (1 N, 30 mL). It was extracted with Et<sub>2</sub>O and the extracts were dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel to give 4,4'-bitolyl (109.1 mg, 0.599 mmol). On the other hand, it was determined that 6.0 mL of this Grignard reagent contained 64.2 mg of 4,4'-bitolyl by independent experiment (hydrolysis of the Grignard reagent). Thus the amount of initially formed 4,4-bitolyl in the reduction step is 44.9 mg (109.1–64.2 = 44.9 mg, 0.246 mmol). The molar ratio of  $Fe(acac)_3/4,4$ '-bitolyl is 1.04, which strongly suggests that catalytic active species is Fe(I)according to the following equation.

$$2ArMgBr + Fe^{III}X_3 \longrightarrow Ar-Ar + 2MgBrX + Fe^{I}X$$

Distribution of products in the reaction of 1a with 2m (Table 1). The reactions were carried out according to the general procedure (vide supra). The crude material was divided into two fractions by column chromatography using silica gel and pentane. The first fraction was composed of alkene 4 and alkane 5. The second fraction was composed of the crosscoupling product **3am** and 4,4'-bitolyl (6). The amount of each component in each fraction was calculated by integral ratio in its <sup>1</sup>H NMR spectrum.

## References

- (1) Charles, R. G.; Pawlikowski, M. A. J. Phys. Chem. 1958, 62, 440.
- (2) Chatti, S; Bortolussi, M; Loupy, A. Tetrahedron 2001, 57, 4365.
- (3) Alnajja, M. S.; Kuivila, H. G. J. Am. Chem. Soc. 1985, 107, 416.
- (4) Van der Mey, M.; Hatzelmann, A.; Van Klink, G. P. M.; Van der Laan, I. J.; Sterk, G. J.; Thibaut, U.; Ulrich, W. R.; Timmerman, H. J. Med. Chem. 2001, 44, 2523.
- (5) Bell, V. L.; Gidding, P. J.; Holmes, A. B.; Mock, G. A.; Raphael, R. A. J. Chem. Soc., Perkin Trans. 1 1986, 1515.