

Supporting Information

for

Suzuki-Miyaura, α -Ketone Arylation and Dehalogenation Reactions Catalyzed by a Versatile (NHC)-Palladacycle (NHC = *N*-Heterocyclic Carbene) Complex

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General Considerations

- All aryl halides and boronic acids were used as received (Aldrich, Acros, Combi-Blocks), as well as the technical grade isopropanol (Mallinckrodt Chemicals). Sodium *tert*-butoxide (Acros) and potassium *tert*-butoxide (Acros) were stored under argon in an MBraun glove box.

- Palladacycle **1** was prepared according to reported procedure.¹
- All reactions were carried out under an atmosphere of argon in screw cap vials.
- Flash chromatography was performed on silica gel 60 (230-400 mesh) using mixtures hexanes:ethylacetate, unless mentioned otherwise.

Suzuki-Miyaura Cross-Coupling of Aryl Chlorides or Triflates with Phenylboronic

Acid. General Procedure: In a glovebox, **1** (2 mol%, 14.6 mg), sodium *tert*-butoxide (1.2 mmol, 115 mg) and phenylboronic acid (1.2 mmol, 146 mg) were added in turn to a vial equipped with a magnetic bar, and closed with a screw cap with a septum. Outside the glove-box, technical grade isopropanol (1.5 mL) was injected into the vial and the mixture stirred on a stirring plate at room temperature for 15 min. Aryl chloride or triflate (1 mmol) was then injected at a rate of 20 μ l/30 sec. The reaction was monitored by gas chromatography. When the reaction reached completion, as gauged by GC analysis, a small amount of silica gel was added to the vial, the solvent was evaporated *in vacuo* and the product isolated by flash chromatography (hexanes/ethyl acetate 10:1) and the purity of the products was determined to be >95% by ¹H NMR. The amount of product reported is the addition of two runs:

3-Nitrobiphenyl (Table 1, entry 8):² The general procedure afforded 366 mg (92 %) of the title compound.

2-Phenylthiophene (Table 3, entry 1):³ The general procedure afforded 240 mg (75 %) of the title compound.

¹ Viciu, M. S.; Kelly, R. A., III; Stevens, E. D.; Naud, F.; Studer, M.; Nolan, S. P. *Org. Lett.* **2003**, 5, 1479-1482.

² Arai, N.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **1995**, 68, 1707-1714.

³ Liu, W.-D.; Chi, C.-C.; Pai, I.-F.; Wu, A.-T.; Chung, W.-S. *J. Org. Chem.* **2002**, 67, 9267-9275.

3-Phenylthiophene (Table 3, entry 2):⁴ The general procedure afforded 251 mg (78 %) of the title compound.

2-Phenylbenzimidazole (Table 3, entry 3):⁵ The general procedure afforded 365 mg (94%) of the title compound.

3-Pyridinylphenyl (Table 3, entry 4):⁶ The general procedure afforded 259 mg (83 %) of the title compound.

2-Pyridinylphenyl (Table 3, entry 5):⁷ The general procedure afforded 282 mg (91 %) of the title compound.

4-Acetylbiphenyl (Table 4, entry 1):⁸ The general procedure afforded 282 mg (91 %) of the title compound.

Biphenyl (Table 4, entry 2):⁹ The general procedure afforded 282 mg (91 %) of the title compound.

4-Methoxybiphenyl (Table 4, entry 3):¹⁰ The general procedure afforded 282 mg (91 %) of the title compound.

1-Phenylnaphthalene (Table 4, entry 4):¹¹ The general procedure afforded 282 mg (91 %) of the title compound.

α -Ketone Arylation with Aryl Halides. *General procedure:* In a glovebox, **1** (0.25 mol%, 1.8 mg), sodium *tert*-butoxide (1.1 mmol, 106 mg) and anhydrous THF (3 mL) were added in turn to a vial equipped with a magnetic bar, and sealed with a screw cap

⁴ Rieke, R. D.; Kim, S.-H.; Wu, X. *J. Org. Chem.* **1997**, *62*, 6921-6927.

⁵ Vaden Eyden, J. J.; Delfosse, F.; Lor, P.; Van Haverbeke, Y. *Tetrahedron* **1995**, *51*, 5813-5818.

⁶ Sakamoto, T.; Kondo, Y.; Murata, N.; Yamanaka, H. *Tetrahedron* **1993**, *49*, 9713- 9720.

⁷ Molander, G. A.; Biolatto, B. *J. Org. Chem.* **2003**, *68*, 4302-4314.

⁸ Barba, I.; Chinchilla, R.; Gómez, C. *Tetrahedron* **1990**, *46*, 7813-7822.

⁹ Littke, A. F.; Dai, D.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020-4028.

¹⁰ Rao, M. S. C.; Rao, G. S. K. *Synthesis* **1987**, 231-233.

¹¹ Kataoka, N.; Shelby, Q.; Stambuli, J. P.; Hartwig, J. F. *J. Org. Chem.* **2002**, *67*, 5553-5566.

fitted with a septum. Outside the glovebox, the ketone (1.1 mmol) and the aryl halide (1 mmol) were injected in turn through the septum. The vial was then stirred on a stirring plate at 70 °C unless otherwise indicated. The reaction was monitored by gas chromatography. When the reaction reached completion, or no further conversion could be observed, water was added to the reaction mixture, the organic layer was extracted with diethyl ether, dried over magnesium sulfate and the solvent was evaporated *in vacuo*. When necessary the product was purified by flash chromatography on silica gel and the purity of the products was determined to be >95% by ¹H NMR. The reported yields are the average of at least two runs:

2-(4-Methylphenyl)-1-phenyl-1-propanone (Table 5, entry 1):¹² The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 95/5), 221 mg (99 %) of the title compound.

1-Phenyl-2-[4-(trifluoromethyl)phenyl]-1-propanone (Table 5, entry 2):¹³ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 9/1), 239 mg (86 %) of the title compound.

2-(4-Methoxyphenyl)-1-phenyl-1-propanone (Table 5, entry 3):¹⁴ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 9/1), 204 mg (85 %) of the title compound.

2-(2-Methylphenyl)-1-phenyl-1-propanone (Table 5, entry 4):¹² The general procedure yielded, after flash chromatography on silica gel (hexane/EtOAc, 95/5), 211 mg (94 %) of the title compound.

¹² Culkin, D. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 5816-5817.

¹³ Nicolaou, K. C.; Montagnon, T.; Baran, P. S.; Zhong, Y.-L. *J. Am. Chem. Soc.* **2002**, *124*, 2245-2258.

¹⁴ Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **1999**, *121*, 1473-1478.

2-(2-Methoxyphenyl)-1-phenyl-1-propanone (Table 5, entry 5):¹⁵ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 9/1), 235 mg (98 %) of the title compound.

2-(Phenyl)acetophenone (Table 5, entry 6):¹⁶ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 9/1), 182 mg (93 %) of the title compound.

2-(2-Methylphenyl)-1-phenylethanone (Table 5, entry 7):¹⁴ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 95/5), 193 mg (92 %) of the title compound.

2-(2-Methoxyphenyl)-1-phenylethanone (Table 5, entry 8):¹⁵ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 8/2), 192 mg (85 %) of the title compound.

2-Phenyl-1-tetralone (Table 5, entry 9):¹⁷ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 9/1), 189 mg (85 %) of the title compound.

2-(2-Methylphenyl)-1-tetralone (Table 5, entry 10):¹⁸ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 9/1), 207 mg (88 %) of the title compound.

2-Phenylcyclohexanone (Table 5, entry 11):¹⁴ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 8/2), 125 mg (72 %) of the title compound. A second fraction (49 mg) containing the title product along with diarylation

¹⁵ Bell, H. C.; Pinhey, J. T.; Sternhell, S. *Aust. J. Chem.* **1982**, *35*, 2237-2245.

¹⁶ Hamann, B. C.; Hartwig, J. F. *J. Am. Chem. Soc.* **1997**, *119*, 12382-12383.

¹⁷ Wang, D. Z.; Kim, Y.-J.; Streitwieser, A. *J. Am. Chem. Soc.* **2000**, *122*, 10754-10760.

¹⁸ Viciu, M. S.; Germaneau, R. F.; Nolan, S. P. *Org. Lett.* **2002**, *4*, 4053-4056.

product [2,5-diphenylcyclohexanone]¹⁹ (1:1.8) was collected.

2,4-Diphenyl-3-pentanone (Table 5, entry 12):²⁰ The above procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 95/5), 214 mg (90 %) of the title compound.

2-Phenyl-3-butanone²¹ and 1-Phenyl-2-butanone:²² (Table 5, entry 13). The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 95/5), 133 mg (90 %) of a mixture of the title compounds. The ratio for the two products was determined by ¹H NMR.

1-(1-Naphthyl)-2-phenylethanone (Table 5, entry 14):²³ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 98/2), 233 mg (95 %) of the title compound.

1-Phenyl-2-(3-pyridinyl)-1-propanone (Table 5, entry 15):¹⁴ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 98/2), 160 mg (76 %) of the title compound.

2-(4-Methylphenyl)-1-phenyl-1-propanone (Table 7, entry 1):¹² The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 95/5), 197 mg (88 %) of the title compound.

2-(4-Methoxyphenyl)-1-phenyl-1-propanone (Table 7, entry 2):¹⁴ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 9/1), 218 mg (91 %) of the title compound.

¹⁹ Tolbert, L. M.; Islam, M. N.; Johnson, R. P.; Loiselle, P. M.; Shakespeare, W. C. *J. Am. Chem. Soc.* **1990**, *112*, 6416-6417.

²⁰ Dolhem, E.; Ocafrain, M.; Nedelec, J. Y.; Troupel, M. *Tetrahedron* **1997**, *53*, 17089-17096.

²¹ Sakai, T.; Matsumoto, S.; Hidaka, S.; Imajo, N.; Tsuboi, S.; Utaka, M. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 3473-3475.

²² This product is commercially available from Aldrich.

²³ Baumgartner, M. T.; Gallego, M. H.; Pierini, A. B. *J. Org. Chem.* **1998**, *63*, 6394-6397.

2-(2-Methylphenyl)-1-phenyl-1-propanone (Table 7, entry 3):¹² The general procedure yielded, after flash chromatography on silica gel (hexane/EtOAc, 95/5), 209 mg (93 %) of the title compound.

2-(2-Methoxyphenyl)-1-phenyl-1-propanone (Table 7, entry 4):¹⁵ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 9/1), 230 mg (96 %) of the title compound.

1-Phenyl-2-(2,4,6-trimethylphenyl)-1-propanone (Table 7, entry 5):²⁴ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 9/1), 234 mg (93 %) of the title compound.

2-Biphenyl-4-yl-1-phenyl-propan-1-one (Table 7, entry 6):²⁵ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 98/2), 255 mg (89 %) of the title compound.

1-(2-Methoxyphenyl)-3,3-dimethyl-2-butanone (Table 7, entry 7):²⁶ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 98/2), 173 mg (90 %) of the title compound.

2-Phenyl-1-tetralone (Table 7, entry 8):¹⁷ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 9/1), 200 mg (90 %) of the title compound.

2-(2-Methylphenyl)-1-tetralone (Table 7, entry 9):¹⁸ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 9/1), 216 mg (92 %) of the title compound.

2-(2-Methoxyphenyl)-1-tetralone (Table 7, entry 10):¹⁸ The general procedure yielded,

²⁴ Wagner, P. J.; Zhou, B. *J. Am. Chem. Soc.* **1988**, *110*, 611-612.

²⁵ García-Garibay, M. A.; Shin, S.; Sanrame, C. N. *Tetrahedron Lett.* **2000**, *56*, 6729-6737.

²⁶ Beugelmans, R.; Ginsburg, H. *J. Chem. Soc., Chem. Commun.* **1980**, *11*, 508-509.

after flash chromatography on silica gel (hexane/ EtOAc, 8/2), 216 mg (92 %) of the title compound.

2-Phenylcyclohexanone (Table 7, entry 11):¹⁴ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 8/2), 207 mg (88 %) of the title compound. A second fraction (23 mg) containing the title product along with diarylation product [2,5-diphenylcyclohexanone⁸] (1:2.4) was collected.

1-(1-Naphthyl)-2-phenylethanone (Table 7, entry 12):²³ The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 98/2), 223 mg (91 %) of the title compound.

Large Scale α -Ketone Arylation with Aryl Halides. *General procedure:* In a glovebox, **1** (0.25 mol%, 18 mg), sodium *tert*-butoxide (11 mmol, 1.06 g) and anhydrous THF (30 mL) were added in turn to a vial equipped with a magnetic bar, and sealed with a screw cap fitted with a septum. Outside the glovebox, the ketone (11 mmol) and the aryl halide (10 mmol) were injected in turn through the septum. The vial was then stirred on a stirring plate at 70 °C unless otherwise indicated. The reaction was monitored by gas chromatography. When reaction reached completion, or no further conversion could be observed, water was added to the reaction mixture, the organic layer was extracted with diethylether, dried over magnesium sulfate and the solvent was evaporated *in vacuo*. When necessary the product was purified by flash chromatography on silica gel until the purity of the products was determined to be >95% by ¹H NMR:

2-(4-Methylphenyl)-1-phenyl-1-propanone (Table 5, entry 1): The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 95/5), 2.06 g (92 %)

of the title compound.

2-(Phenyl)-acetophenone (Table 5, entry 6): The general procedure yielded, after flash chromatography on silica gel (hexane/ EtOAc, 9/1), 1.77 g (90 %) of the title compound.

Microwave-Assisted α -Ketone Arylation with Aryl Halides. Microwaved-assisted reactions were carried out in an Emrys™ Optimizer microwave reactor kindly supplied by Personal Chemistry Inc. (now Biotage). *General procedure:* In a drybox, **1** (0.25 mol%, 1.8 mg), sodium *tert*-butoxide (1.1 mmol, 106 mg) and anhydrous THF (3 mL) were added in turn to a microwave vial (supplied by Personal Chemistry Inc.) equipped with a magnetic bar, and sealed with a cap fitted with a septum. Outside the drybox, the ketone (1.1 mmol) and the aryl halide (1.0 mmol) were injected in turn through the septum. The vial was then placed in a microwave reactor and the temperature set at 130 °C. In the apparatus, the desired temperature was reached in 10 sec and held constant for 2 min, and subsequently the vial was cooled to room temperature with a flow of air. The mixture was then analyzed by gas chromatography. GC and conversions are average of two runs.

Catalytic Dehalogenation of Aryl Chlorides. *General Procedure:* In a glovebox, **1** (1 mol%, 7.3 mg), potassium *tert*-butoxide (1.2 mmol, 134.7 mg) were added in turn to a vial equipped with a magnetic bar, and closed with a screw cup with a septum. Outside the glovebox, technical grade isopropanol (2 mL) was injected into the vial and the mixture stirred on a stirring plate at room temperature for 15 min, and aryl chloride (1 mmol) was then injected. The reactions were monitored by gas chromatography and product identity compared with authentic samples.