Palladium Charcoal-Catalyzed Suzuki-Miyaura Coupling to Obtain Arylpyridines and Arylquinolines

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Supporting Information:

Experimental :

All reactions were conducted under a nitrogen atmosphere. NMR spectra were recorded in $CDCl_3$ (^1H at 400 MHz and ^{13}C at 100MHz). All starting materials were obtained commercially. Compounds **1a-c**, **1f**, **1g**, **1i**, **1j-m 4a, 4b**, **5**, **8** and **10** were purchased from Tokyo Kasei Kogyo Co., Ltd. Compound **1e** was purchased from Koei Chemical Co., Ltd. Compound **1h** was purchased from Wako Pure Chemical Industries, Ltd. Compound **4c** was purchased from Sigma-Aldrich Co. All reagents and solvents were commercial grade. NE Chemcat STD 5% Pd/C (water content 54%) was used as Pd(0)/C, and Degussa E 106 NE/W 5% Pd/C (water content 53%), Degussa E 106 NE/W 10% Pd/C (water content 51%), or Degussa E 105 CA/W 5% Pd/C(water content 56%) was used as Pd(II)/C.

Method 1. General Procedure for Coupling without Additives in the Presence of Pd(0)/C.

To a solution of 2-bromopyridine (420 mg, 2.66 mmol) and phenylboronic acid (608 mg, 3.99 mmol) in DME (10 mL) were added 2M Na_2CO_3 (5 mL) and NE Chemcat STD

5% Pd/C (water content 54%)(545 mg, 0.12 mmol), and the reaction mixture was then stirred at 80 ºC for 9 hours. After filtration, the catalyst was washed four times with AcOEt (15 mL). The combined organic layers were washed with 10% NaOHaq and brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (hexane:AcOEt=5:1) to give the product **3a** (213 mg, 54% yield).

Yields of **3b-f** are given in Table 1. Compounds **3a-c** are commercially available from Tokyo Kasei Kogyo Co., Ltd. Compounds **3d-f**,[3a)-c)] are described in the literature.

Method 2. General Procedure for Coupling with TBAB in the Presence of Pd(0)/C.

To a solution of 2-bromopyridine (420 mg, 2.66 mmol), phenylboronic acid (608 mg, 3.99 mmol) and TBAB (86 mg, 0.27 mmol) in DME (10 mL) were added 2M Na_2CO_3 (5 mL) and NE Chemcat STD 5% Pd/C (water content 54%)(545 mg, 0.12 mmol), and the reaction mixture was then stirred at 80 ºC for 9 hours. After filtration, the catalyst was washed four times with AcOEt (15 mL). The combined organic layers were washed with 10% NaOHaq and brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (hexane:AcOEt=5:1) to give the product **3a** (350 mg, 85% yield).

The equivalents of TBAB and the yields of products **3b-f** are given in Table 1.

Method 3. General Procedure for Coupling with PPh_3

To a solution of 2-bromopyridine (420 mg, 2.66 mmol), phenylboronic acid (405 mg, 3.3 mmol) and PPh_3 (122 mg, 0.47 mmol) in DME (10 mL) were added 2M Na_2CO_3 (5 mL) and NE Chemcat STD 5% Pd/C (water content 54%)(545 mg, 0.12 mmol), and the reaction mixture was stirred at 80 ºC for 9 hours. After filtration, the water layer was extracted twice with AcOEt (30 mL). The combined organic layers were washed with 10% NaOHaq and brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (hexane:AcOEt=5:1) to give the product **3a** (350 mg, 85% yield).

Yields of **3a-j**, **6a-c**, **7** are given in Table 2. Compound **6a** is commercially available Sigma-Aldrich Co. and **3g-j** [6a)-d)], **6b** [6e)], **6c**[6f)] and **7** [6g)] are described in the literature.

Method 4. General Procedure for Coupling with PPh_3 in the presence of Pd(II)/C

To a solution of 2-chloro-6-methoxypyridine (382 mg, 2.66 mmol), phenylboronic acid (405 mg, 3.3 mmol) and PPh_3 (122 mg, 0.47 mmol) in DME (10 mL) were added 2M Na_2CO_3 (5 mL) and Degussa E 106 NE/W 10% Pd/C (water content 51%)(259 mg, 0.12 mmol), and the reaction mixture was stirred at 80 ℃ for 9 hours. After filtration, the water layer was extracted twice with AcOEt (30 mL). The combined organic layers were washed with 10% NaOHaq and brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (hexane:AcOEt=5:1) to give the product **3a** (443 mg, 90% yield).

In the reaction of **1k**, Degussa E 106 NE/W 5% Pd/C (water content 53 %)(545 mg, 0.12 mmol) was used instead of Degussa E 106 NE/W 10% Pd/C (water content 51%)(259 mg, 0.12 mmol). In the reactions of **1l-m**, **4c**, and **8**, Degussa E 105 CA/W 5% Pd/C (water content 56%)(545 mg, 0.12 mmol) was used instead of Degussa E 106 NE/W 10% Pd/C (water content 51%)(259 mg, 0.12 mmol). The yields of **3i, 3j** and **9** are given in Table 3. Compound **9** is commercially available from Tokyo Kasei Kogyo Co., Ltd.

Method 5. The reaction with dppb, dppp or 2-(dicyclohexylphosphino)biphenyl in the presence of Pd(0)/C

To a solution of 3-chloropyridine (302mg, 2.66 mmol), phenylboronic acid (405 mg, 3.3 mmol) and dppb (98 mg, 0.23 mmol) in DME (10 mL) were added 2M Na_2CO_3 (5 mL) and NE Chemcat STD 5% Pd/C (water content 54%)(545 mg, 0.12 mmol), and the reaction mixture was stirred at 80 ºC for 9 hours. When the reaction was checked by HPLC, no desired product was observed, and only the peak of the starting material was seen in the chart. When dppp (95 mg, 0.23 mmol) was used instead of dppb, the same result was obtained.

To a solution of 3-chloropyridine (302mg, 2.66 mmol), phenylboronic acid (405 mg, 3.3 mmol) and -(dicyclohexylphosphino)biphenyl (82 mg, 0.23 mmol) in DME (10 mL) were added 2M Na_2CO_3 (5 mL) and NE Chemcat STD 5% Pd/C (water content 54%)(545 mg, 0.12 mmol). After filtration, the water layer was extracted twice with AcOEt (30 mL). The combined organic layers were washed with 10% NaOHaq and brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography (hexane:AcOEt=5:1) to give the product **3a** (363 mg, 88% yield). Yields of **3b**, **3c**, and **6c** are given in Table 4.

Method 6. The reaction with 2-(dicyclohexylphosphino)biphenyl in the presence of Pd(II)/C

To a solution of 4-methoxyphenylchloride (379 mg, 2.66 mmol), phenylboronic acid (405 mg, 3.3 mmol) and 2-(dicyclohexylphosphino)biphenyl (82 mg, 0.23 mmol) in DME (10 mL) were added 2M Na_2CO_3 (5 mL) and Degussa E 105 CA/W 5% Pd/C (water content 56%)(545 mg, 0.12 mmol), and the reaction mixture was stirred at 80 °C for 9 hours. After filtration, the catalyst was washed four times with AcOEt. The combined organic layers were washed with 10%NaOHaq and brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure to recover 4-methoxybiphenyl (**11**) (392 mg, 80% yield). Compound **11** is commercially available from Tokyo Kasei Kogyo Co., Ltd.