Palladium-Catalyzed Coupling Reaction of Terminal Alkynes with Aryl Iodides in the Presence of Indium Tribromide and Its Application to a One-Pot Synthesis of 2-Phenylindole

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Experimental Section

General Methods. All reactions were carried out under an Ar atmosphere, unless otherwise noted. Piperidine was freshly distilled from CaH_2 prior to use. Toluene was dried over sodium/benzophenone and distilled. Reactions were monitored by GC analysis of reaction aliquots. Analytical GC was carried out on a Shimadzu GC-14A gas chromatograph equipped with a fused capillary column. GC yields were determined using decane as the internal standard. Thin-layer chromatography (TLC) was carried out on silica gel 60 F_{254} (MERCK), and compounds were detected by UV light. Column chromatography was performed using Silica gel 60 (Merck). ^1H NMR (500MHz) and ^{13}C NMR (125MHz) spectra were recorded with a JEOL ECP-500 spectrometer in CDCl_3 . The compounds reported herein are known compounds and were identified by ^1H NMR and ^{13}C NMR by comparison with literature data.

General Procedure for the Pd-In Catalyzed Cross-Coupling Reaction. To a suspension of

indium tribromide powder (0.02 mmol) in piperidine (0.5 mL) was added a solution of the terminal alkyne **1** (0.48 mmol) in piperidine (0.5 mL) via syringes, and the mixture was stirred for 2.5 h at room temperature. A piperidine solution (1 mL) of the aryl iodide **2** (0.4 mmol) and $\text{PdCl}_2(\text{PPh}_3)_2$ (0.02 mmol) was also stirred for the same time. To the former solution was added the latter solution via a cannula. The resulting mixture was stirred at room temperature or 60 °C (bath temperature), and monitored by GC analysis until the starting material was consumed. The reaction was quenched with a saturated aqueous solution of NaHCO_3 . The aqueous layer was extracted with Et_2O , the organic phases were dried over anhydrous Na_2SO_4 , filtered, and evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane : AcOEt = 9:1) to afford the corresponding cross-coupling product **3**.

General Procedure for the Intramolecular Cyclization of 4. To a 10 mL recovery flask under argon containing a freshly distilled toluene (2 mL) were added 2-phenylethynylaniline (**3ad**, 0.4 mmol) and indium tribromide (0-0.4 mmol). The resulting mixture was refluxed and monitored by GC analysis until the starting material was consumed. After the usual work-up, the crude product was purified by silica gel column chromatography (hexane : AcOEt = 7:3) to afford 2-phenylindole (**4**) as a colorless solid in yields as described in Table 3.

General Procedure for the One-Pot Synthesis of 4. To a suspension of indium tribromide powder (0.02 mmol) in piperidine (0.5 mL) was added a solution of phenylacetylene (**1a**, 0.48 mmol) in piperidine (0.5 mL) via syringes, and the mixture was stirred for 2.5 h at room temperature. A solution of the *o*-iodoaniline (**2d**, 0.4 mmol) and $\text{PdCl}_2(\text{PPh}_3)_2$ (0.02 mmol) in piperidine (1 mL) was also stirred at the same temperature for the same time. To the former solution was added the latter solution via a cannula. The resulting mixture was stirred at room temperature. After 1h, the mixture was cooled, and the solvent was replaced by toluene (2 mL).

To the toluene solution containing the coupling product was added additional indium tribromide (0.4 mmol), and the resulting mixture was refluxed and monitored by GC analysis until the coupling product was consumed. The reaction was quenched with a saturated aqueous solution of NaHCO_3 . The aqueous layer was extracted with Et_2O , the organic phases were dried over anhydrous Na_2SO_4 , filtered, and evaporated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane : AcOEt = 7:3) to afford 42mg (54%) of 2-phenylindole (**4**) as a colorless solid.

The products prepared are already known.

4-(Phenylethynyl)toluene (3aa):¹ colorless crystals; IR(KBr) 2217 cm^{-1} ($\text{C}\equiv\text{C}$); ^1H NMR (500MHz, CDCl_3) δ 2.36 (s, 3H), 7.14 (d, 2H, $J = 8\text{ Hz}$), 7.32 (m, 3H), 7.42 (d, 2H, $J = 8\text{ Hz}$), 7.52 (d, 2H, $J = 6.5\text{ Hz}$); ^{13}C NMR (125MHz, CDCl_3) δ 21.5, 88.7, 89.6, 120.2, 123.5, 128.1, 128.3, 129.1, 131.5, 131.6, 138.4.

2-(Phenylethynyl)toluene (3ab):² colorless oil; IR(CCl_4) 2214 cm^{-1} ($\text{C}\equiv\text{C}$); ^1H NMR (500MHz, CDCl_3) δ 2.40 (s, 3H), 7.08 (m, 3H), 7.22 (m, 3H), 7.42 (m, 3H); ^{13}C NMR (125MHz, CDCl_3) δ 20.7, 88.3, 93.3, 122.9, 123.5, 125.5, 128.1, 128.2, 128.3, 129.4, 131.5, 131.8, 140.1.

4-(Phenylethynyl)aniline (3ac):³ colorless needles from CH_2Cl_2 -hexane; IR(KBr) 2213 cm^{-1} ($\text{C}\equiv\text{C}$); ^1H NMR (500MHz, CDCl_3) δ 3.80 (brs, 2H), 6.62 (d, 2H, $J = 8\text{ Hz}$), 7.30 (m, 5H), 7.50 (d, 2H, $J = 8\text{ Hz}$); ^{13}C NMR (125MHz, CDCl_3) δ 87.3, 90.1, 112.5, 114.7, 123.8, 127.6, 128.2, 131.3, 132.9, 146.6.

2-(Phenylethynyl)aniline (3ad):⁴ pale yellow prisms from CH_2Cl_2 -hexane; IR(KBr) 2207 cm^{-1} ($\text{C}\equiv\text{C}$); ^1H NMR (500MHz, CDCl_3) δ 4.32 (brs, 2H), 6.72 (t, 2H, $J = 8.5\text{ Hz}$), 7.13 (t, 1H, $J = 8\text{ Hz}$), 7.35 (m, 4H), 7.52 (d, 2H, $J = 8\text{ Hz}$); ^{13}C NMR (125MHz, CDCl_3) δ 85.9, 94.8, 108.1, 114.5, 118.2, 123.3, 128.3, 128.4, 129.8, 131.5, 132.2, 147.6.

4-(Phenylethynyl)anisole (3ae):⁵ colorless solid; IR(KBr) 2215 cm⁻¹ (C≡C); ¹H NMR (500MHz, CDCl₃) δ 3.81 (s, 3H), 6.88 (d, 2H, *J* = 8.5 Hz), 7.33 (m, 3H), 7.48 (d, 2H, *J* = 8.5 Hz), 7.53 (m, 2H); ¹³C NMR (125MHz, CDCl₃) δ 55.7, 88.5, 89.9, 114.4, 115.8, 124.1, 128.4, 128.8, 131.9, 133.5, 160.1.

4-(Phenylethynyl)nitrobenzene (3af):⁶ pale yellow needless; IR(KBr) 2160 cm⁻¹ (C≡C) ; ¹H NMR (500MHz, CDCl₃) δ 7.38 (m, 3H), 7.54 (m, 2H), 7.64 (d, 2H, *J* = 8.7 Hz), 8.20 (d, 2H, *J* = 8.7 Hz); ¹³C NMR (125MHz, CDCl₃) δ 87.5, 94.7, 122.1, 123.6, 128.5, 129.2, 130.2, 131.8, 132.2, 146.9.

4-(Fluorophenyl)phenylacetylene (3ag):⁷ colorless needless from CH₂Cl₂-hexane; IR(KBr) 2217 cm⁻¹ (C≡C); ¹H NMR (500MHz, CDCl₃) δ 7.04 (t, 2H, *J* = 8.5 Hz), 7.34 (m, 3H), 7.51 (m, 4H); ¹³C NMR (125MHz, CDCl₃) δ 88.3, 89.0, 115.6 (d, *J* = 21.9 Hz), 119.4 (d, *J* = 3.9 Hz), 123.1, 128.3 (d, *J* = 4.8 Hz), 131.5, 133.4 (d, *J* = 7.6 Hz), 162.5 (d, *J* = 248.0 Hz).

4-(Octynyl)toluene (3ba):⁸ yellow oil; IR(CCl₄) 2199 cm⁻¹ (C≡C); ¹H NMR (500MHz, CDCl₃) δ 0.90 (t, 3H, *J* = 7 Hz), 1.32 (m, 4H), 1.44 (q, 2H, *J* = 7 Hz), 1.58 (q, 2H, *J* = 7 Hz), 2.32 (s, 3H), 2.38 (t, 2H, *J* = 7 Hz), 7.07 (d, 2H, *J* = 8 Hz), 7.28 (d, 2H, *J* = 8 Hz); ¹³C NMR (125MHz, CDCl₃) δ 14.1, 19.4, 21.4, 22.6, 28.6, 28.8, 31.4, 80.5, 89.6, 121.0, 128.9, 131.4, 137.3.

4-(Octynyl)nitrobenzene (3bf):⁸ yellow oil; IR(CCl₄) 2218 cm⁻¹ (C≡C); ¹H NMR (500MHz, CDCl₃) δ 0.88 (t, 3H, *J* = 7.5 Hz), 1.30 (m, 4H), 1.43 (q, 2H, *J* = 7.5 Hz), 1.60 (q, 2H, *J* = 7.5 Hz), 2.42 (t, 2H, *J* = 7.5 Hz), 7.48 (d, 2H, *J* = 8.5 Hz), 8.12 (d, 2H, *J* = 8.5 Hz); ¹³C NMR (125MHz, CDCl₃) δ 14.0, 19.6, 22.5, 28.4, 28.6, 31.3, 79.3, 96.8, 123.5, 131.2, 132.2, 146.6.

4-(Trimethylsilylethynyl)anisole (3ce):⁹ colorless oil; IR(CCl₄) 2137 cm⁻¹ (C≡C); ¹H NMR (500MHz, CDCl₃) δ 0.22 (s, 9H), 3.77 (s, 3H), 6.79 (d, 2H, *J* = 8.5 Hz); ¹³C NMR (125MHz, CDCl₃) δ 0.0, 55.1, 92.3, 105.2, 115.2, 123.7, 133.3, 159.7.

2-(Trimethylsilylethynyl)aniline (3cd):¹⁰ pale yellow oil; IR(CCl₄) 2139 cm⁻¹ (C≡C); ¹H NMR (500MHz, CDCl₃) δ 0.24 (s, 9H), 4.03 (brs, 2H), 6.65 (td, 1H, *J* = 7.8, 1.2 Hz), 6.69 (d, 1H, *J* = 7.8 Hz), 7.09 (td, 1H, *J* = 7.8, 1.5 Hz), 7.27 (td, 1H, *J* = 7.8, 1.2 Hz); ¹³C NMR (125MHz, CDCl₃) δ 0.1, 99.8, 101.7, 108.1, 114.4, 118.0, 129.9, 132.3, 147.8.

4-(Trimethylsilylethynyl)nitrobenzene (3cf):¹¹ yellow solid; IR(KBr) 2159 cm⁻¹ (C≡C); ¹H NMR (500MHz, CDCl₃) δ 0.25 (s, 9H), 7.57 (d, 2H, *J* = 8.5 Hz), 8.14 (d, 2H, *J* = 8.5 Hz); ¹³C NMR (125MHz, CDCl₃) δ -0.32, 100.6, 102.7, 123.5, 130.0, 132.7, 147.2.

4-(*t*-Butylethynyl)nitrobenzene (3df):¹² brown solid; IR(KBr) 2237 cm⁻¹ (C≡C); ¹H NMR (500MHz, CDCl₃) δ 1.31 (s, 9H), 7.47 (d, 2H, *J* = 8.5 Hz), 8.11 (d, 2H, *J* = 8.5 Hz); ¹³C NMR (125MHz, CDCl₃) δ 28.2, 30.7, 77.9, 104.6, 123.4, 131.2, 132.2, 146.6.

2-(Phenylethynyl)thiophene (3ah):¹³ white solid; IR(KBr) 2203 cm⁻¹ (C≡C); ¹H NMR (500MHz, CDCl₃) δ 7.01 (dd, 1H, *J* = 4.8, 3.9 Hz), 7.28 (m, 2H), 7.34 (m, 3H), 7.53 (m, 2H); ¹³C NMR (125MHz, CDCl₃) δ 82.6, 93.0, 127.1, 127.2, 128.3, 128.4, 131.4, 131.8.

2-Phenylindole (4):¹⁴ pale yellow solid; IR(KBr) 3451 cm⁻¹ (NH); ¹H NMR (500MHz, CDCl₃) δ 6.83 (s, 1H), 7.13 (t, 1H, *J* = 7.5 Hz), 7.20 (t, 1H, *J* = 7.5 Hz), 7.32 (t, 1H, *J* = 7.5 Hz), 7.39 (d, 1H, *J* = 7.5 Hz), 7.43 (t, 2H, *J* = 7.5 Hz), 7.64 (t, 3H, *J* = 7.5 Hz), 8.34 (brs, 1H); ¹³C NMR (125MHz, CDCl₃) δ 100.0, 110.9, 120.3, 120.7, 122.4, 125.2, 127.7, 129.0, 129.3, 132.4, 136.9, 137.9.

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