# A Highly Regioselective Sonogashira Coupling as a Key Step in the Preparation of the First Phenanthroline with Two Diverse Reactive Groups in 3,8-Positions

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## Experimental Section

**Materials and General Procedures.** 3,8-Dibromo-1,10-phenanthroline[1] and 2-bromo-1,3-dimethoxybenzene[2] were prepared according to literature procedures. All other chemicals were commercially available and used without further purification. The solvents were distilled before use. $^1$H NMR spectra were recorded on Bruker AC 200 (200 MHz) spectrometers (using the deuterated solvent as the lock and residual solvent as the internal reference). IR spectra were recorded on a Perkin-Elmer (1750 FT-IR). Microanalyses were carried out with a Carlo Erba Elemental Analyzer 1106. Melting points were determined by using a Büchi SMP-20 and are uncorrected. Electrospray mass spectra (ES-MS) were recorded on a TSQ 7000 Triple-Quadrupol-Tandem-Mass spectrometer (Finnigan MAT) with Finnigan ESI-Interface. Data recording and evaluation was carried out using the ICIS 8.1 software package (Finnigan MAT).

*2-(2,6-Dimethoxyphenyl)-3,8-dibromo-1,10-phenanthroline* (**6**): Under argon, a solution of 2-bromo-1,3-dimethoxybenzene (1.6 g, 7.5 mmol) in 50 ml of dry diethyl ether was combined with a 2.5 M solution of n-butyllithium in n-hexane (3 ml, 7.5 mmol). After stirring for 5 h at room temperature 3,8-dibromo-1,10-phenanthroline (**2**) was added (1.4 g, 4 mmol), whereupon a dark-brown mixture was

formed. After stirring overnight at room temperature, it was hydrolyzed with water (100 ml) and the mixture was extracted with dichloromethane (4 × 50 ml). Manganese dioxide (1.8 g, 20 mmol) was added to the combined organic layers and the mixture was stirred for 1.5 h at room temperature, then finally dried over $MgSO_4$. After filtration, the solvents were distilled off at the rotary evaporator, and the residue was washed with n-hexane (3 × 50 ml), then purified by chromatography (silica gel: $CHCl_3$). After washing the crude product with n-hexane (3 × 50 ml), phenanthroline **6** [$R_f$ ($CH_2Cl_2$/Aceton 20:1) = 0.25, 0.99 g] was isolated in 50% yield. m.p. > 230 °C (decompose). – IR (KBr, $cm^{-1}$): $\tilde{\nu}$ = 2933 (w), 2835 (w), 1591 (s, C=C), 1474 (s, C=C), 1432 (s), 1393 (m), 1289 (m), 1251 (s), 1109 (s), 1024 (m), 782 (s, Ar-H), 736 (m, Ar-H). – $^1$H NMR (200 MHz, $CDCl_3$): δ = 3.71 (s, 6H, OMe), 6.68 (d, *J* = 8.6 Hz, 2H, 3′-H, 5′-H), 7.33 (t, *J* = 8.6 Hz, 1H, 4′-H), 7.74 (d, *J* = 8.8 Hz, 1H, 6-H), 7.81 (d, *J* = 8.8 Hz, 1H, 5-H), 8.37 (d, *J* = 2.4 Hz, 1H, 7-H), 8.51 (s, 1H , 4-H), 9.17 (d, *J* = 2.4 Hz, 1H, 9-H). – $^{13}$C NMR (200 MHz, $CDCl_3$) : δ = 55.9 ($OCH_3$), 104.0, 119.7, 123.4, 126.3, 126.9, 128.8, 129.7, 130.2, 130.3, 137.4, 138.7, 142.5, 145.3, 151.4, 153.5, 158.3. – $C_{20}H_{24}Br_2N_2O_2$ (474.15.45): calcd. C 50.66, H 2.98, N 5.91, found: C 50.56, H 3.20, N 5.81. – ESI-MS: $[^{12}C_{20}{}^{1}H_{15}{}^{79}Br^{81}Br\,{}^{14}N_2{}^{16}O_2]^+$ calcd: 475.0, found: 475.0.

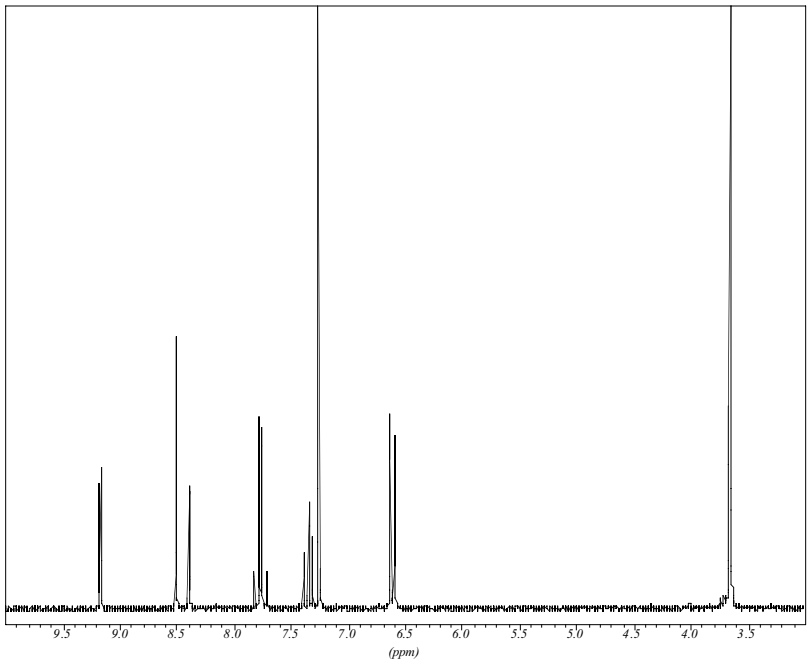


**Figure 1**: $^1$H NMR spectrum of **6** in $CDCl_3$ at room temperature.

*2-(2,6-Dimethoxyphenyl)-3-trimethylsilylethynyl-8-bromo-1,10-phenanthroline* (**7**): To a stirred solution of 2-(2,6-dimethoxyphenyl)-3,8-dibromo-1,10-phenanthroline (0.7 g, 1.5 mmol), $PdCl_2(PPh_3)_2$ (53 mg, 75 μmol) and CuI (29 mg, 150μmol) in dry benzene (50 ml) was added 0.64 ml of dry triethylamine (4.5 mmol) followed by trimethylsilylacetylene (TMS) (0.31ml, 2.25 mmol) at room temperature under argon in a screw cap tube. The vessel was capped and heated to 90°C for two days under argon. The solvent was removed under reduced pressure. The black residue was dissolved in 130 ml of dichloromethane, washed with a 2% aqueous KCN (3 × 50 ml) and water (3 × 50 ml), and dried over $MgSO_4$. Careful flash chromatography on silica gel ($CH_2Cl_2$) afforded analytically pure phenanthroline **7** [$R_f$ ($CH_2Cl_2$/acetone 20:1) = 0.49, 0.4 g] in 55% yield. m.p. > 300 °C (dec.). – IR (KBr, $cm^{-1}$): $\tilde{\nu}$ = 2956 (m), 2835 (m), 2151 (m, C≡C), 1600 (s), 1587 (s), 1474 (s), 1434 (s), 1393 (s), 1291 (m), 1251 (s), 1176 (m), 1110 (s), 1081 (m), 1026 (m), 982 (m), 842 (s, Ar-H), 784 (s, Ar-H), 737 (m, Ar-H), 647 (m). – $^1$H NMR (200 MHz, $CDCl_3$): δ = 0.32 (s, 9H, $Si(CH_3)_3$), 3.69 (s, 6H, OMe), 6.57 (d, *J* = 8.0 Hz, 2H, 3′-H, 5′-H), 7.34 (t, *J* = 8.0 Hz, 1H, 4′-H), 7.83 (s, 2H, 5-H, 6-H), 8.42 (s, 1H, 4-H), 8.53 (s, 1H, 7-H), 9.23 (s, 1H, 9-H). – $^{13}$C NMR (200 MHz, $CDCl_3$) : δ = -0.21 (Si-$CH_3$), 55.8 ($OCH_3$), 99.6, 100.6, 104.0, 119.4, 123.9, 125.6, 126.5, 126.8, 127.8, 129.2, 130.2, 138.5, 139.8, 142.2, 144.0, 151.6, 155.9, 158.0. – $C_{25}H_{23}BrN_2O_2Si$ (491.45): calcd. C 61.10, H 4.72, N 5.70, found: C 60.76, H 4.60, N 5.56. – ES-MS: $[^{12}C_{25}{}^{1}H_{24}{}^{79}Br^{14}N_2{}^{16}O_2{}^{28}Si]^+$ calcd: 491.0, found: 491.2.

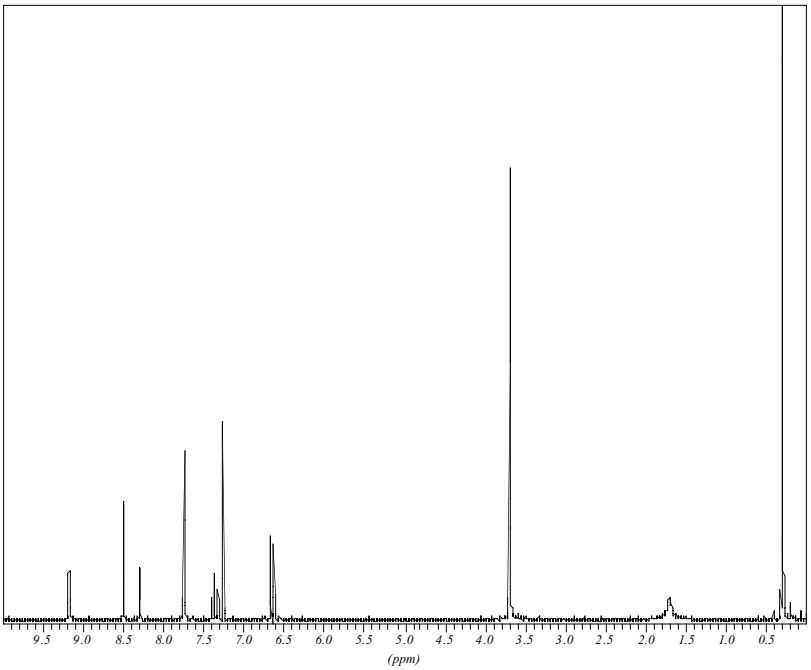


**Figure 2**: $^1$H NMR spectrum of **7** in $CDCl_3$ at room temperature (signal at 1.7 ppm for $H_2O$).

*2,9-Bis(2,6-dimethoxyphenyl)-3-trimethylsilylethynyl-8-bromo-1,10-phenanthroline* (**8**): Under argon, a solution of 2-bromo-1,3-dimethoxybenzene (0.65 g, 3.0 mmol) in 50 ml of dry diethyl ether was combined with a 2.5 M solution of n-butyllithium in n-hexane (1.2 ml, 3.0 mmol) and stirred for 5 h at room temperature. Then 2-(2,6-dimethoxyphenyl)-3-trimethylsilylethynyl-8-bromo-1,10-phenanthroline (**7**) (0.5 g, 1.01 mmol) was added. The deep-red mixture was stirred overnight at room temperature. After hydrolysis with 50 ml of water, the mixture was extracted with dichloromethane (4 × 50 ml). Manganese dioxide (0.45 g, 5 mmol) was added to the combined organic layers and the mixture was stirred for 3 h at room temperature, then dried over $MgSO_4$. After filtration, the solvents were distilled off by rotary evaporation and the residue was purified by chromatography (silica gel: $CHCl_3$) to furnish 0.42 g (68%) of phenanthroline **8** [$R_f$ ($CH_2Cl_2$/acetone 20:1) = 0.73]. m.p. > 240 °C (dec.). – IR (KBr, cm$^{-1}$): $\tilde{\nu}$ = 2956 (m), 2835 (m), 2149 (m, C≡C), 1599 (s), 1591 (s), 1473 (s), 1432 (s), 1402 (s), 1286 (m), 1250 (s), 1174 (m), 1112 (s), 1034 (m), 1000 (m), 860 (s, Ar-H), 782 (s, Ar-H), 721 (m, Ar-H), 648 (m). – $^1$H NMR (200 MHz, $d_6$-DMSO, $CDCl_3$) : δ = 0.04 (s, 9H, $Si(CH_3)_3$ ), 3.69 (s, 12H, OMe), 6.58 (d, *J* = 8.4 Hz, 2H, 3″-H, 5″-H), 6.61 (d, *J* = 8.4 Hz, 2H, 3′-H, 5′-H), 7.33 (t, *J* = 8.4 Hz, 2H, 4′-H, 4″-H), 7.70 (d, *J* = 8.6 Hz, 1H, 6-H), 7.76 (d, *J* = 8.6 Hz, 1H, 5-H), 8.35 (s, 1H, 4-H),

8.48 (s, 1H, 7-H). – $^{13}$C NMR (200 MHz, DMSO-$d_6$) : δ = 0.99 (Si-$CH_3$), 57.0 (-$OCH_3$), 101.5, 103.8, 105.6, 121.6, 123.3, 123.8, 127.5, 128.2, 128.7, 130.7, 131.5, 131.9, 140.0, 145.0, 147.2, 156.1, 158.8, 159.0. – $C_{33}H_{31}BrN_2O_4Si{\cdot}0.5H_2O$ (636.61): calcd. C 62.26, H 5.07, N 4.40, found C 62.17, H 4.90, N 4.32. – ES-MS: $[^{12}C_{33}{}^{1}H_{32}{}^{79}Br^{14}N_2{}^{16}O_4{}^{28}Si]^+$ calcd: 627.0, found: 627.2.

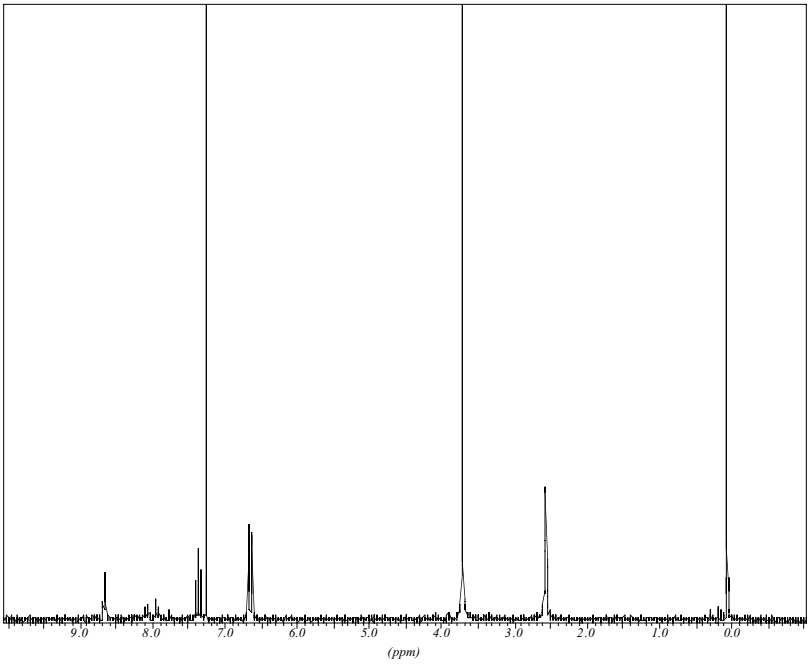


**Figure 3**: $^{1}$H NMR spectrum of **8** in $d_6$-DMSO + $CDCl_3$ at room temperature.

*2,9-Bis(2,6-dimethoxyphenyl)-3-ethynyl-8-bromo-1,10-phenanthroline* (**1** ): To a solution of phenanthroline **8** (170 mg, 271 μmol) in THF (20 ml) a 1 N solution of KOH in MeOH (23 ml) was added. The reaction mixture was stirred at room temperature for 3 h, treated with a saturated aqueous solution of $NH_4Cl$ (40 ml). The organic layer was collected, while the water layer was extracted with dichloromethane (4 × 30 ml). The combined organic layers were dried over $MgSO_4$ overnight. Concentration in vacuum afforded a residue, which was purified by chromatography (silica gel: 1. hexane, 2. $CH_2Cl_2$) to give 0.12 g phenanthroline **1** (80%) [$R_f$ ($CH_2Cl_2$/acetone 20:1) = 0.73]. m.p. > 270 °C (dec.). –IR (KBr, $cm^{-1}$): $\tilde{\nu}$ = 3284, 2965, 2938, 2838, 1592 (s), 1473 (s), 1429 (s), 1401 (s), 1287 (m), 1250 (s), 1174 (m), 1111 (s), 1034 (m), 920 (m), 782 (s, Ar-H), 731 (m, Ar-H). – $^{1}$H NMR (200 MHz, $CD_2Cl_2$) : δ = 3.15 (s, 1 H, ≡ C-H), 3.69 (s, 12H, OMe), 6.66 (d, $J$ = 8.4 Hz, 2H, 3′-H, 5′-

H), ), 6.67 (d, $J$ = 8.4 Hz, 2H, 3″-H, 5″-H), 7.38 (t, $J$ = 8.4 Hz, 1H, 4′-H), 7.40 (t, $J$ = 8.4 Hz, 1H, 4″-H), 7.81 (d, $J$ = 8.9 Hz, 1H, 6-H) 7.82 (d, $J$ = 8.9 Hz, 1H, 5-H), 8.44 (s, 1H, 7-H), 8.53 (s, 1H, 4-H). – $^{13}$C NMR(200 MHz, $C_2DCl_2$) : δ = 56.3 (-$OCH_3$), 82.1, 104.1, 104.2, 120.3, 125.8, 126.3, 127.3, 127.9, 129.8, 130.5, 132.4, 137.3, 139.0, 141.1, 147.8, 152.8, 158.3, 158.5. – $C_{30}H_{23}BrN_2O_4 \cdot H_2O$ (573.4): calcd. C 62.84, H 4.39, N 4.88; found: C 62.66, H 4.20, N 4.61. – ES-MS: $[^{12}C_{30}{}^{1}H_{24}{}^{79}Br^{14}N_2{}^{16}O_4]^+$ calcd: 555.0, found: 555.2.

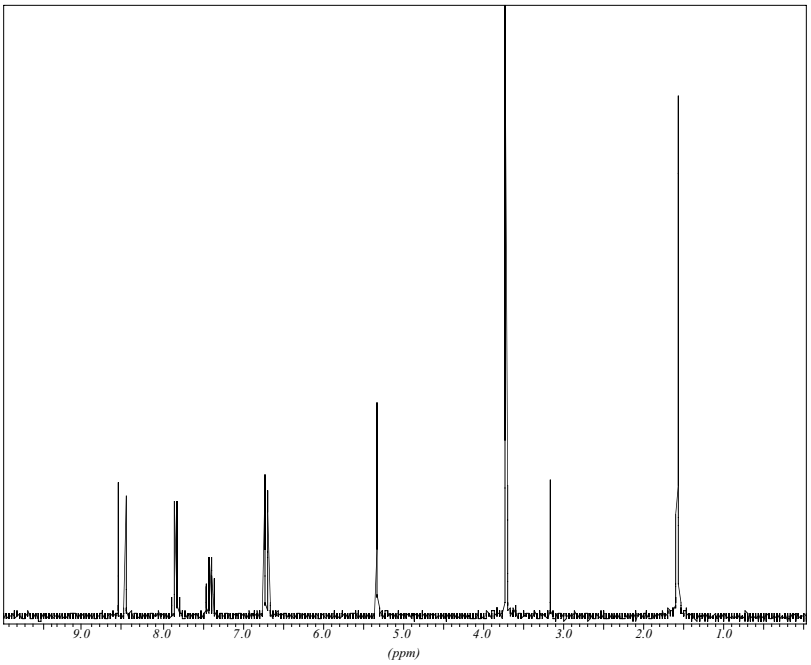


**Figure 4**: $^{1}$H NMR spectrum of **1** in $CD_2Cl_2$ at room temperature (signal at 1.6 ppm for $H_2O$).

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