Functionalized 2,2'-Bipyridines and 2,2':6',2''-Terpyridines via Stille-Type Cross-Coupling Procedures

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Supporting Information on spectral characterization data of all new compounds.

Methyl-substituted 2,2'-bipyridines (4-12), general procedure: A mixture of 2-tributylstannyl-methylpyridine **3a-c** or 2-tributylstannyl-pyridine (27.0 mmol) **3d**, 2-bromopicoline **2a-c** (23.0 mmol) and *tetrakis*(triphenylphosphine)-palladium(0) (0.95 g, 0.82 mmol) in 65 ml toluene was refluxed under nitrogen for 48 h. The resulting brown mixture was evaporated *in vacuo* and the dark, muddy liquid was dissolved in dichloromethane. The organic phase was washed with aqueous HCl (3 × 20 ml, 6 M). To remove the product from solution the combined aqueous layers were transferred drop wise in aqueous ammonia (10%) under cooling. The resulting oil was extracted with CH₂Cl₂ (3 × 30 ml). The organic phases were washed with ammonia and water and the solvent was removed *in vacuo*. The resulting suspension was purified by column chromatography.

6-Methyl-2,2'-bipyridine (4): ¹H NMR (CDCl₃): δ = 2.52 (s, 3 H), 7.03 (d, *J* = 7.63 Hz, 1 H), 7.15 (m, 1 H), 7.57 (t, *J* = 8.01 Hz, 1 H), 7.66 (m, 1 H), 8.07 (d, *J* = 8.01 Hz, 1 H), 8.30 (d, *J* = 7.63 Hz, 1 H), 8.56 (m, 1 H). ¹³C NMR (CDCl₃): δ = 25.0, 118.4, 121.5, 123.6, 123.8, 137.1, 137.4, 149.5, 155.9, 156.9, 158.3. GCMS (EI, 70 eV): *m/z* (%) = 170 (100) [M⁺]. Anal. Calcd for C₁₁H₁₀N₂: C, 77.62; H, 5.92; N, 16.46. Found: C, 77.20; H, 5.96; N, 16.21.

5-Methyl-2,2'-bipyridine (5): ¹H NMR (CDCl₃): δ = 2.27 (s, 3 H), 7.16 (m, 1 H), 7.50 (d, *J* = 7.50 Hz, 1 H), 7.67 (m, 1 H), 8.19 (d, *J* = 8.01 Hz, 1 H), 8.26 (d, *J* = 8.01 Hz, 1 H), 8.40 (s, 1 H), 8.56 (d, *J* = 4.58 Hz, 1 H). ¹³C NMR (CDCl₃): δ = 18.7, 120.9, 121.1, 123.7, 133.7, 137.2, 137.8, 149.4, 150.0, 154.0, 156.7. GCMS (EI, 70 eV): *m/z* (%) = 170 (100) [M⁺]. Anal. Calcd for C₁₁H₁₀N₂: C, 77.62; H, 5.92; N, 16.46. Found: C, 77.79; H, 5.92; N, 16.34.

4-Methyl-2,2'-bipyridine (6): ¹H NMR (CDCl₃): δ = 2.36 (s, 3 H), 7.06 (d, *J* = 4.96 Hz, 1 H), 7.23 (m, 1 H), 7.73 (m, 1 H), 8.16 (s, 1 H), 8.32 (d, *J* = 8.01 Hz, 1 H), 8.46 (d, *J* = 4.57 Hz, 1 H), 8.60 (m, 1 H). ¹³C NMR (CDCl₃): δ = 21.5, 121.6, 122.2, 123.9, 125.0, 137.2, 148.4, 149.3, 149.4, 156.3, 156.7. GCMS (EI, 70 eV): *m/z* (%) = 170 (100) [M⁺]. Anal. Calcd for C₁₁H₁₀N₂: C, 77.62; H, 5.92; N, 16.46. Found: C, 77.30; H, 5.85; N, 16.35.

6,6'-Dimethyl-2,2'-bipyridine (7): ^1H NMR (CDCl_3): δ = 2.56 (s, 6 H), 7.08 (d, J = 7.63 Hz, 2 H), 7.61 (dd, J = 7.63, 8.01 Hz, 2 H), 8.11 (d, J = 7.63 Hz, 2 H). ^{13}C NMR (CDCl_3): δ = 25.0, 118.6, 123.4, 137.4, 156.3, 158.2. GCMS (EI, 70 eV): m/z (%) = 184 (100) [M^+]. Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{N}_2$: C, 78.23; H, 6.57; N, 15.21. Found: C, 78.11; H, 6.56; N, 15.12.

5,5'-Dimethyl-2,2'-bipyridine (8): ^1H NMR (CDCl_3): δ = 2.37 (s, 6 H), 7.60 (dd, J = 8.2, 2.1 Hz, 2 H), 8.24 (d, J = 8.0 Hz, 2 H), 8.48 (s, 2 H). ^{13}C NMR (CDCl_3): δ = 18.3, 120.3, 133.0, 137.4, 149.5, 153.7. GCMS (EI, 70 eV): m/z (%) = 184 (100) [M^+]. Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{N}_2$: C, 78.23; H, 6.57; N, 15.21. Found: C, 78.08; H, 6.46; N, 15.14.

4,4'-Dimethyl-2,2'-bipyridine (9): ^1H NMR (CDCl_3): δ = 2.37 (s, 6 H), 7.06 (d, J = 4.96 Hz, 2 H), 8.16 (s, 2 H), 8.46 (d, J = 4.96 Hz, 2 H). ^{13}C NMR (CDCl_3): δ = 21.6, 122.4, 125.0, 148.6, 149.2, 156.3. GCMS (EI, 70 eV): m/z (%) = 184 (100) [M^+]. Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{N}_2$: C, 78.23; H, 6.57; N, 15.21. Found: C, 77.91; H, 6.46; N, 14.88.

4,6'-Dimethyl-2,2'-bipyridine (10): M.p. 41 °C. ^1H NMR (CDCl_3): δ = 2.37 (s, 3 H), 2.56 (s, 3 H), 7.03 (d, J = 4.96 Hz, 1 H), 7.08 (d, J = 7.63 Hz, 1 H), 7.61 (t, J = 7.82 Hz, 1 H), 8.08 (d, J = 7.63 Hz, 1 H), 8.16 (s, 1 H), 8.45 (d, J = 4.96 Hz, 1 H). ^{13}C NMR (CDCl_3): δ = 21.9, 25.0, 118.7, 122.3, 123.6, 124.9, 137.4, 148.4, 149.3, 156.1, 156.6, 158.2. GCMS (EI, 70 eV): m/z (%) = 184 (100) [M^+]. Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{N}_2$: C, 78.23; H, 6.57; N, 15.21. Found: C, 77.92; H, 6.66; N, 15.05.

5,6'-Dimethyl-2,2'-bipyridine (11): M.p. 51 °C. ^1H NMR (CDCl_3): δ = 2.38 (s, 3 H), 2.63 (s, 3 H), 7.14 (d, J = 7.63 Hz, 1 H), 7.60 (m, 1 H), 7.68 (t, J = 8.01 Hz, 1 H), 8.14 (d, J = 8.01 Hz, 1 H), 8.28 (m, 1 H), 8.49 (s, 1 H). ^{13}C NMR (CDCl_3): δ = 18.7, 25.0, 118.2, 121.1, 123.3, 133.6, 137.4, 137.8, 149.9, 154.3, 156.0, 158.2. GCMS (EI, 70 eV): m/z (%) = 184 (100) [M^+]. Anal. Calcd for $\text{C}_{12}\text{H}_{12}\text{N}_2$: C, 78.23; H, 6.57; N 15.21. Found: C, 78.24; H, 6.92; N, 14.83.

4,5'-Dimethyl-2,2'-bipyridine (12): M.p. 54 °C. ¹H NMR (CDCl₃): δ = 2.37 (s, 3 H), 2.42 (s, 3 H), 7.10 (m, 1 H), 7.60 (m, 1 H), 8.18 (s, 1 H), 8.25 (m, 1 H), 8.43 (m, 1 H), 8.45 (m, 1 H). ¹³C NMR (CDCl₃): δ = 18.7, 21.5, 121.1, 122.0, 124.8, 133.7, 137.9, 148.5, 149.2, 149.9, 154.1, 156.4. GCMS (EI, 70 eV): *m/z* (%) = 184 (100) [M⁺]. Anal. Calcd for C₁₂H₁₂N₂: C, 78.23; H, 6.57; N, 15.21. Found: C, 78.24; H, 6.76; N, 15.03.

5-Bromomethyl-2,2'-bipyridine (13): ¹H NMR (CDCl₃): δ = 4.66 (s, 2 H), 7.44 (m, 1 H), 7.94 (d, *J* = 7.45 Hz, 1 H), 7.96 (m, 1 H), 8.52 (d, *J* = 8.01 Hz, 1 H), 8.54 (m, 1 H), 8.80 (s, 1 H), 8.81 (d, *J* = 4.58 Hz, 1 H). ¹³C NMR (CDCl₃): δ = 31.3, 120.8, 121.1, 123.7, 133.9, 1367.0, 137.4, 149.2, 150.1, 153.9, 156.7. Anal. Calcd for C₁₁H₉BrN₂: C, 53.04; H, 3.64; N, 11.25. Found: C, 53.40; H, 3.53; N, 11.42.

6,6''-Dimethyl-2,2':6',2''-terpyridine (15): Yield: 43% (route B) as white crystals. M.p. 171 °C. ¹H NMR (CDCl₃): δ = 2.65 (s, 6 H), 7.18 (d, *J* = 7.63 Hz, 2 H), 7.73 (t, *J* = 7.63 Hz, 2 H), 7.93 (t, *J* = 8.01 Hz, 1 H), 8.41 (d, *J* = 7.63 Hz, 2 H), 8.47 (d, *J* = 8.01 Hz, 2 H). ¹³C NMR (CDCl₃): δ = 25.0, 118.5, 121.2, 123.6, 137.3, 138.1, 155.9, 156.1, 158.1. GCMS (EI, 70 eV): *m/z* (%) = 261 (100) [M⁺]. Anal. Calcd for C₁₇H₁₅N₃: C, 78.13; H, 5.79; N, 16.08. Found: C, 78.42; H, 5.63; N, 16.16.

5,5''-Dimethyl-2,2':6',2''-terpyridine (16): Yield: 90% (route A), 69% (route B) as white crystals. M.p. 173 °C. ¹H NMR (CDCl₃): δ = 2.39 (s, 6 H), 7.63 (dd, *J* = 8.01, 2.28 Hz, 2 H), 7.91 (t, *J* = 7.82 Hz, 1 H), 8.38 (d, *J* = 7.62 Hz, 2 H), 8.49 (d, *J* = 8.40 Hz, 2 H), 8.50 (s, 2 H). ¹³C NMR (CDCl₃): δ = 18.3, 120.3, 120.6, 133.3, 137.3, 137.7, 149.4, 153.7, 155.3. GCMS (EI, 70 eV): *m/z* (%) = 261 (100) [M⁺]. Anal. Calcd for C₁₇H₁₅N₃: C, 78.13; H, 5.79; N, 16.08. Found: C, 77.92; H, 5.73; N, 16.07.

4,4''-Dimethyl-2,2':6',2''-terpyridine (17): Yield: 50% (route A), 52% (route B) as white crystals. M.p. 186 °C. ¹H NMR (CDCl₃): δ = 2.39 (s, 6 H), 7.17 (dd, *J* = 4.96, 0.77 Hz, 2 H), 7.94 (t, *J* = 8.01 Hz, 1 H), 8.41 (s, 2 H), 8.42 (d, *J* = 8.01 Hz, 2 H), 8.56 (d, *J* = 4.95 Hz, 2 H).

^{13}C NMR (CDCl_3): δ = 21.7, 121.5, 122.2, 125.1, 138.1, 148.3, 149.3, 155.9, 156.4. GCMS

(EI, 70 eV): m/z (%) = 261 (100) [M^+]. Anal. Calcd for $\text{C}_{17}\text{H}_{15}\text{N}_3$: C, 78.13; H, 5.79; N, 16.08.

Found: C, 78.04; H, 6.00; N, 15.92.

2,6-Dichloro-isonicotinic-methylester (19): 2,6-Dichlorisonicotinic acid chloride (5.00 g, 24 mmol) is added slowly to dry methanol (50 ml). The mixture is stirred for 2 h at room temperature. After removal of the methanol *in vacuo*, the white residue is dissolved in chloroform (30 ml), washed with aqueous Na_2CO_3 (10 ml, 5%), water (10 ml) and brine (10 ml) and dried over Na_2SO_4 . After removal of the solvent, the white product (4.55 g, 92%) can be used without further purification. ^1H NMR (CDCl_3): δ = 3.98 (s, 3 H), 7.81 (s, 2 H). ^{13}C NMR (CDCl_3): δ = 53.6, 123.0, 142.7, 151.8, 163.5. Anal. Calcd for $\text{C}_7\text{H}_5\text{Cl}_2\text{NO}_2$: C, 40.81; H, 2.45; N, 6.80. Found: C, 41.13; H, 2.41; N, 6.70.

2,6-Dichloro-isonicotinic-ethylester (20): 2,6-Dichlorisonicotinic acid chloride (5.00 g, 24 mmol) is added slowly to dry ethanol (50 ml). The work-up is carried out according to the procedure described for **19** to yield 4.75 g, 90% of compound **20**. ^1H NMR (CDCl_3): δ = 1.39 (t, 3 H, J = 7.23 Hz), 4.40 (q, 2H, J = 7.08 Hz), 7.70 (s, 2 H). ^{13}C NMR (CDCl_3): δ = 14.4, 63.0, 123.0, 143.1, 151.8, 163.0. Anal. Calcd for $\text{C}_8\text{H}_7\text{Cl}_2\text{NO}_2$: C, 43.66; H, 3.21; N, 6.37. Found: C, 43.90; H, 3.13; N, 6.35.

5,5''-Dimethyl-2,2':6',2''-terpyridine-4'-methylester (21): M.p. 157 °C. ^1H NMR (CDCl_3): δ = 2.40 (s, 6 H), 3.98 (s, 3 H), 7.63 (m, 2 H), 8.47 (d, J = 8.2 Hz, 2 H), 8.53 (m, 2 H), 8.90 (s, 2 H). ^{13}C NMR (CDCl_3): δ = 18.8, 52.9, 120.1, 121.2, 134.2, 137.7, 139.93, 150.1, 153.4, 157.0, 166.3. GCMS (EI, 70 eV): m/z (%) = 319 (40) [M^+], 261 (100) [$\text{M}^+ - 58$]. Anal. Calcd for $\text{C}_{19}\text{H}_{17}\text{N}_3\text{O}_2$: C, 71.46; H, 5.37; N, 13.16. Found: C, 71.62; H, 5.42; N, 12.91.

5,5''-Dimethyl-2,2':6',2''-terpyridine-4'-ethylester (22): M.p. 245 °C. ^1H NMR (CDCl_3): δ = 1.41 (t, J = 6.90 Hz, 3 H), 2.35 (s, 6 H), 4.43 (q, J = 6.90 Hz, 2 H), 7.59 (d, J = 8.01 Hz, 2 H), 8.42 (d, J = 8.02 Hz, 2 H), 8.49 (s, 2 H), 8.90 (s, 2 H). ^{13}C NMR (CDCl_3): δ = 14.7, 18.7,

62.0, 120.0, 121.1, 134.1, 137.7, 140.3, 150.0, 153.4, 156.9, 165.8. GCMS (EI, 70 eV): m/z (%) = 333 (100) [M^+]. Anal. Calcd for $C_{20}H_{19}N_3O_2$: C, 72.05; H, 5.74; N, 12.60. Found: C, 72.42; H, 5.44; N, 12.83.

4'-Hydroxymethyl-5,5''-dimethyl-2,2':6',2''-terpyridine (23): M.p. 249 °C. 1H NMR ($CDCl_3$): δ = 2.37 (s, 6 H), 3.63 (s, 1 H), 4.81 (s, 2 H), 7.60 (m, 2 H), 8.32 (s, 2 H), 8.42 (d, J = 7.98 Hz, 2 H), 8.46 (s, 2 H). ^{13}C NMR ($CDCl_3$): δ = 18.7, 64.1, 118.3, 121.3, 133.8, 137.8, 149.7, 152.8, 154.0, 155.8. GCMS (EI, 70 eV): m/z (%) = 291 (90) [M^+], 290 (100) [M^+-1]. UV/VIS (CH_3CN): λ_{max}/nm ($\epsilon/(L \times mol^{-1} \times cm^{-1})$) = 287 (29800). Anal. Calcd for $C_{18}H_{17}N_3O$: C, 74.20; H, 5.88; N, 14.42. Found: C, 73.84; H, 5.90; N, 14.40.

2,6-Dichloro-4-hydroxymethylpyridine (24): M.p. 136 °C. 1H NMR (d_6 -DMSO): δ = 4.55 (d, J = 5.52 Hz, 2 H), 5.70 (t, J = 5.73 Hz, 1 H), 7.43 (s, 2 H). ^{13}C NMR (d_6 -DMSO): δ = 61.1, 120.8, 149.4, 159.9. GCMS (EI, 70 eV): m/z (%) = 177 (70) [M^+-1], 142 (100) [M^+-35]. Anal. Calcd for $C_6H_5Cl_2NO$: C, 40.48; H, 2.83; N, 7.87. Found: C, 40.50; H, 2.50; N, 7.47.

2,6-Dichloro-4-(*t*-butyldimethylsiloxy)methylpyridine (25): M.p. 136 °C. 1H NMR (d_6 -DMSO): δ = 0.10 (s, 6 H), 0.93 (s, 9 H), 4.68 (s, 2 H), 7.19 (s, 2 H). ^{13}C NMR (d_6 -DMSO): δ = 5.0, 18.7, 26.2, 63.1, 120.1, 150.8, 157.2. GCMS (EI, 70 eV): m/z (%) = 291 (65) [M^+], 276 (100) [M^+-15]. Anal. Calcd for $C_{12}H_{19}Cl_2NOSi$: C, 49.31; H, 6.55; N, 4.79. Found: C, 49.68; H, 6.40; N, 4.52.

4'-(*t*-Butyldimethylsilyloxymethyl)-5,5''-dimethyl-2,2':6',2''-terpyridine (26): Yield (Route A: 80%, route B: 59%). M.p. 137 °C. 1H NMR ($CDCl_3$): δ = 0.13 (s, 6 H), 0.96 (s, 9 H), 2.49 (s, 6 H), 4.82 (s, 2 H), 7.66 (dd, J = 8.01, 1.52 Hz, 2 H), 8.36 (s, 2 H), 8.49 (d, J = 8.01 Hz, 2 H), 8.52 (s, 2 H). ^{13}C NMR ($CDCl_3$): δ = 4.8, 18.7, 26.3, 64.2, 118.2, 121.3, 133.8, 137.8, 149.7, 152.7, 154.1, 155.8. GCMS (EI, 70 eV): m/z (%) = 405 (20) [M^+], 390 (100) [M^+-15]. Anal. Calcd for $C_{24}H_{31}N_3OSi$: C, 71.01; H, 7.70; N, 10.36. Found: C, 70.82; H, 7.90; N, 10.11.

5,5''-Bis(bromomethyl)-2,2':6',2''-terpyridine-4'-methylester (27): Yield: 10%. M.p. 132

°C. ^1H NMR (CDCl_3): δ = 4.02 (s, 3 H), 4.57 (s, 4 H), 7.92 (m, 2 H), 8.60 (d, J = 8.2 Hz, 2 H), 8.75 (m, 2 H), 9.00 (s, 2 H). ^{13}C NMR (CDCl_3): δ = 29.8, 53.1, 121.2, 121.6, 134.6, 138.0, 140.2, 149.7, 155.5, 156.3, 166.0. GCMS (EI, 70 eV): m/z (%) = 477 (100) [M^+]. Anal. Calcd for $\text{C}_{19}\text{H}_{15}\text{Br}_2\text{N}_3\text{O}_2$: C, 47.83; H, 3.17; N, 8.81. Found: C, 48.01; H, 3.20; N, 9.10.

5,5''-Bis(bromomethyl)-2,2':6',2''-terpyridine-4'-ethylester (28): Yield: 72%. M.p. 143 °C.

^1H NMR (CDCl_3): δ = 1.44 (t, J = 6.06 Hz, 3 H), 4.47 (q, J = 7.06 Hz, 2 H), 4.55 (s, 4 H), 7.89 (dd, J = 8.20, 2.28 Hz, 2 H), 8.56 (d, J = 8.20 Hz, 2 H), 8.72 (s, 2 H), 9.00 (s, 2 H). ^{13}C NMR (CDCl_3): δ = 14.74, 29.9, 62.2, 121.6, 134.6, 136.4, 137.9, 140.6, 146.6, 149.8, 155.70, 165.6. GCMS (EI, 70 eV): m/z (%) = 491 (100) [M^+]. Anal. Calcd for $\text{C}_{20}\text{H}_{17}\text{Br}_2\text{N}_3\text{O}_2$: C, 48.91; H, 3.49; N, 8.56. Found: C, 49.72; H, 3.20; N, 8.92.

5,5''-Bis(acetoxymethyl)-2,2':6',2''-terpyridine-4'-ethylester (29): Yield: 71%. M.p. 231

°C. ^1H NMR (CDCl_3): δ = 1.42 (t, J = 6.06 Hz, 3 H), 2.10 (s, 6 H), 4.45 (q, J = 7.06 Hz, 2 H), 5.17 (s, 4 H), 7.83 (dd, J = 8.01, 2.20 Hz, 2 H), 8.50 (d, J = 8.02 Hz, 2 H), 8.57 (s, 2 H), 8.90 (s, 2 H). ^{13}C NMR (CDCl_3): δ = 14.7, 21.2, 53.8, 63.9, 120.9, 121.3, 136.4, 136.3, 140.5, 149.5, 15.6, 156.3, 165.6, 171.2. GCMS (EI, 70 eV): m/z (%) = 449 (100) [M^+], 390 (40) [M^+ - 59]. Anal. Calcd for $\text{C}_{24}\text{H}_{23}\text{N}_3\text{O}_6$: C, 64.13; H, 5.16; N, 9.35. Found: C, 64.55; H, 4.80; N, 9.01.

2,6-Dichloro-4-hydroxymethylpyridine (24): To a suspension of LiAlH_4 (2.4 g, 64 mmol) in abs. THF (20 ml), 2,6-dichloro-isonicotinic acid ethylester **20** (20.0 g, 96 mmol) in THF (160 ml) was added slowly at $-20\text{ }^\circ\text{C}$. After 2 h the suspension is allowed to warm to room temperature. After addition of brine (60 ml) and phase separation, the aqueous phase is extracted with CH_2Cl_2 ($2 \times 50\text{ ml}$). After drying and removal of the solvent, the product is purified by column chromatography (SiO_2 , hexane:ethylacetate 1:1) to yield a white solid (7.4 g, 43%). M.p. $136\text{ }^\circ\text{C}$. ^1H NMR (d_6 -DMSO): $\delta = 4.55$ (d, $J = 5.52\text{ Hz}$, 2 H), 5.70 (t, $J = 5.73\text{ Hz}$, 1 H), 7.43 (s, 2 H).

2,6-Dichloro-4-(*t*-butyldimethylsiloxy)methylpyridine (25): A mixture of 2,6-dichloro-4-hydroxymethylpyridine **24** (5.5 g, 31 mmol), TBDMSCl (5.6 g, 3.7 mmol), imidazole (5.08 g, 74 mmol) and 4-dimethylaminopyridine (0.3 g) in abs. DMF (40 ml) is stirred 24 h at $40\text{ }^\circ\text{C}$. After addition of aqueous NaHSO_4 (150 ml, 1 M) and diethyl ether (200 ml) the phases are separated and the aqueous phase was extracted twice with diethyl ether. After washing with brine, drying and removal of the solvent, the desired product is obtained. Crystallization is done from ethyl acetate to yield white crystals of the desired product (8.0 g, 89%). M.p. $136\text{ }^\circ\text{C}$. ^1H NMR (d_6 -DMSO): $\delta = 0.10$ (s, 6 H), 0.93 (s, 9 H), 4.68 (s, 2 H), 7.19 (s, 2 H).