Synthesis of 2,2'-Bipyrroles and 2,2'-Thienylpyrroles from Donor-acceptor Cyclopropanes and 2-Cyanoheteroles

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Supporting Information

Experimental Details: All reactions were run under an atmosphere of argon unless otherwise indicated. Flasks were oven or flamed-dried and allowed to cool in dry box or desiccator prior to use. Solvents and reagents were purified by the standard methods.¹ The ¹H, ¹³C NMR data was obtained on a Varian INOVA 400 spectrometer. For ¹H NMR, chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane and are, in all cases, referenced to the residual proton resonance peaks: δ 7.24 for CHCl₃. The ¹³C NMR chemical shifts were reported in ppm relative to the center peak of the multiplet for deuterated solvents: δ 77.0 (t) for CDCl₃. ¹³C spectra was routinely run with broadband ¹H decoupling. Coupling constants for all spectra are reported in Hertz (Hz). Infrared spectra were measured on a NEXUS 470 FT-IR spectrometer as thin films on sodium bromide plates and are recorded in units of cm⁻¹. HRMS (CI) were made with a VG analytical ZAB2-E instrument.

General Procedure A: To a solution of cyclopropane (2.0 mmol) and 2-cyano-pyrrole (1.0 mmol) in CH₃NO₂ (4.0 mL) at -25 °C was added trimethylsilyl trifluoromethanesulfonate (TMSOTf) (1.5 mmol). The mixture was stirred at -25 °C for 0.5-4.0 h until TLC indicated complete consumption of starting 2-cyano-pyrrole. The resulting mixture was poured into vigorously stirred saturated aqueous NaHCO₃ (10 mL). After 2 min the mixture was extracted with EtOAc (3 × 8 mL). The combined organic solution was washed with H₂O (8 mL), brine (6 mL) and dried (MgSO₄). After filtration through a small pad of celite, volatiles were removed under reduced pressure. The product was purified by chromatography on silica gel using appropriate combination of hexanes-EtOAc for elution.

¹ Armarego, W.L.F.; Perrin, D. D. *Purification of Laboratory Chemicals*; 4th Ed.; Oxford ; Boston : Butterworth Heinemann, 1996.

General Procedure B: To a solution of cyclopropane (2.0 mmol) and 2-thiophenecarbonitrile (1.0 mmol) in $\text{C}_2\text{H}_5\text{NO}_2$ (4.0 mL) at $-25\text{ }^\circ\text{C}$ was added trimethylsilyl trifluoromethanesulfonate (TMSOTf) (1.5 mmol). The mixture was stirred at $-25\text{ }^\circ\text{C}$ for 0.5-1.5 h until TLC indicated complete consumption of starting 2-cyano-thiophene and poured into a vigorously stirred solution of saturated aqueous NaHCO_3 (10 mL). The work up followed the same procedure as described in procedure A.

5-Methyl-1H,1'H-[2,2']bipyrrolyl-3-carboxylic acid ethyl ester (table 1, entry 1)

The title compound was prepared from the corresponding cyclopropane and 1H-pyrrole-2-carbonitrile according to the general procedure A ($0\text{ }^\circ\text{C}$, CH_3NO_2 , 25 min). Purification by flash chromatography on silica gel with 20:1 hexanes-EtOAc for elution gave the title compound as colorless syrup (231 mg, 78%).

R_f 0.61 (25% EtOAc/hexanes);

IR (thin film) ν 3610-3130, 1670 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 12.11 (s, br, 1H), 8.39 (s, br, 1H), 6.85 (t, $J = 2.0$ Hz, 1H), 6.40 (td, $J = 1.3, 1.3$ Hz, 1H), 6.29 (d, $J = 2.0$ Hz, 1H), 6.27-6.24 (m, 1H), 4.32 (q, $J = 7.2$ Hz, 2H), 2.22 (s, 3H), 1.38 (t, $J = 7.2$ Hz, 3H);

^{13}C NMR (100 MHz, CDCl_3) δ 167.0, 130.6, 126.6, 124.1, 118.4, 108.9, 108.6, 108.5, 104.2, 60.1, 14.3, 12.5;

HRMS m/z calcd for $\text{C}_{12}\text{H}_{15}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 219.1134, found: 219.1139.

3',4'-Diethyl-5-methyl-1H,1'H-[2,2']bipyrrolyl-3-carboxylic acid ethyl ester (table 1, entry 2)

The title compound was prepared from the corresponding cyclopropane and 3,4-diethyl-1H-pyrrole-2-carbonitrile according to the general procedure A ($-10\text{ }^\circ\text{C}$, CH_3NO_2 , 45 min). Purification by flash chromatography on silica gel with 20:1 hexanes-EtOAc for elution gave the title compound as colorless syrup (112 mg, 82%).

R_f 0.56 (15% EtOAc/hexanes);

IR (thin film) ν 3450-3210, 1670 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 11.83 (s, br, 1H), 8.28 (s, br, 1H), 6.63 (d, $J = 2.7$ Hz, 1H), 6.34 (dd, $J = 1.0, 1.0$ Hz, 1H), 4.28 (q, $J = 7.2$ Hz, 2H), 2.71 (q, $J = 7.5$ Hz, 2H), 2.50 (q, $J = 7.5$ Hz, 2H), 2.28 (s, 3H), 1.36 (t, $J = 7.2$ Hz, 3H), 1.26 (t, $J = 7.5$ Hz, 3H), 1.23 (t, $J = 7.5$ Hz, 3H);

^{13}C NMR (100 MHz, CDCl_3) δ 166.9, 131.6, 125.9, 125.6, 120.8, 119.7, 114.8, 109.0, 108.8, 60.0, 18.7, 18.1, 15.4, 14.9, 14.4, 12.8;

HRMS m/z calcd for $\text{C}_{16}\text{H}_{23}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 275.1760, found: 275.1757.

1*H*,1'*H*-[2,2']Bipyrrolyl-3-carboxylic acid ethyl ester (table 1, entry 3)

The title compound was prepared from the corresponding cyclopropane and 1*H*-pyrrole-2-carbonitrile according to the general procedure A (−45 °C, C₂H₅NO₂, 4.5 h). Purification by flash chromatography on silica gel with 20:1 hexanes-EtOAc for elution gave the title compound as colorless syrup (130 mg, 41%).

R_f 0.71 (25% EtOAc/hexanes);

¹H NMR (400 MHz, CDCl₃) δ 12.11 (s, br, 1H), 8.52 (s, br, 1H), 6.88-6.86 (m, 1H), 6.63 (t, *J* = 2.0 Hz, 1H), 6.61 (t, *J* = 2.0 Hz, 1H), 6.42-6.41 (m, 1H), 6.26 (q, *J* = 2.0 Hz, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 166.9, 131.5, 123.9, 118.6, 116.6, 111.6, 109.1, 108.8, 104.7, 60.3, 14.4;

HRMS *m/z* calcd for C₁₁H₁₃N₂O₂ [M+H]⁺ 205.0977, found: 205.0967.

3',4'-Diethyl-1*H*,1'*H*-[2,2']bipyrrolyl-3-carboxylic acid ethyl ester (table 1, entry 4)

The title compound was prepared from the corresponding cyclopropane and 3,4-diethyl-1*H*-pyrrole-2-carbonitrile according to the general procedure A (−40 °C, C₂H₅NO₂, 3 h). Purification by flash chromatography on silica gel with 15:1 hexanes-EtOAc for elution gave the title compound as colorless syrup (147 mg, 45%).

R_f 0.56 (15% EtOAc/hexanes);

IR (thin film) ν 3580-3050, 1670 cm^{−1};

¹H NMR (400 MHz, CDCl₃) δ 11.85 (s, br, 1H), 8.60 (s, br, 1H), 6.67 (d, *J* = 2.8 Hz, 2H), 6.63 (d, *J* = 2.4 Hz, 1H), 4.30 (q, *J* = 7.5 Hz, 2H), 2.70 (q, *J* = 7.5 Hz, 2H), 2.49 (q, *J* = 7.5 Hz, 2H), 1.36 (t, *J* = 7.0 Hz, 3H), 1.24 (t, *J* = 7.5 Hz, 3H), 1.22 (t, *J* = 7.5 Hz, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 166.9, 132.4, 125.8, 121.3, 119.6, 116.2, 115.1, 111.7, 109.1, 60.2, 18.6, 18.1, 15.6, 14.9, 14.4;

HRMS *m/z* calcd for C₁₅H₂₁N₂O₂ [M+H]⁺ 261.1603, found: 261.1596.

5-Ethyl-4-methyl-1*H*,1'*H*-[2,2']bipyrrolyl-3-carboxylic acid ethyl ester (table 1, entry 5)

The title compound was prepared from the corresponding cyclopropane and 1*H*-pyrrole-2-carbonitrile according to the general procedure A (−10 °C, CH₃NO₂, 45 min). Purification by flash chromatography on silica gel with 20:1 hexanes-EtOAc for elution gave the title compound as colorless syrup (231 mg, 82%).

R_f 0.68 (25% EtOAc/hexanes);

^1H NMR (400 MHz, CDCl_3) δ 11.99 (s, br, 1H), 8.13 (s, br, 1H), 6.83 (ddd, $J = 5.6, 3.2, 3.2$ Hz, 1H), 6.36-6.34 (m, 1H), 6.23 (dd, $J = 6.2, 2.6$ Hz, 1H), 4.31 (q, $J = 7.2$ Hz, 2H), 2.56 (q, $J = 7.6$ Hz, 2H), 2.16 (s, 3H), 1.37 (t, $J = 7.2$ Hz, 3H), 1.18 (t, $J = 7.6$ Hz, 3H);

^{13}C NMR (100 MHz, CDCl_3) δ 168.0, 130.0, 129.6, 124.5, 118.1, 115.7, 108.8, 108.6, 104.2, 60.0, 18.9, 14.4, 14.3, 11.6;

HRMS m/z calcd for $\text{C}_{14}\text{H}_{19}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 247.1447, found: 247.1443.

5,3',4'-Triethyl-4-methyl-1H,1'H-[2,2']bipyrrolyl-3-carboxylic acid ethyl ester (table 1, entry 6)

The title compound was prepared from the corresponding cyclopropane and 3,4-diethyl-1H-pyrrole-2-carbonitrile according to the general procedure A (0 °C, CH_3NO_2 , 45 min). Purification by flash chromatography on silica gel with 20:1 hexanes-EtOAc for elution gave the title compound as colorless solid (410 mg, 85%).

R_f 0.51 (15% EtOAc/hexanes);

^1H NMR (400 MHz, CDCl_3) δ 11.19 (s, br, 1H), 8.18 (s, br, 1H), 6.59 (d, $J = 2.4$ Hz, 1H), 4.38 (q, $J = 7.2$ Hz, 2H), 2.66 (q, $J = 7.5$ Hz, 2H), 2.59 (q, $J = 7.5$ Hz, 2H), 2.49 (q, $J = 7.5$ Hz, 2H), 2.17 (s, 3H), 1.35 (t, $J = 7.2$ Hz, 3H), 1.23 (t, $J = 7.2$ Hz, 3H), 1.22 (t, $J = 7.5$ Hz, 3H), 1.20 (t, $J = 7.5$ Hz, 3H);

^{13}C NMR (100 MHz, CDCl_3) δ 167.8, 130.3, 129.0, 125.5, 120.9, 120.1, 115.3, 114.4, 109.5, 59.9, 18.63, 18.55, 18.2, 15.6, 14.8, 14.4, 13.8, 11.5;

HRMS m/z calcd for $\text{C}_{18}\text{H}_{27}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 303.2073, found: 303.2072.

4-Methyl-1H,1'H-[2,2']bipyrrolyl-3-carboxylic acid ethyl ester (table 1, entry 7)

The title compound was prepared from the corresponding cyclopropane and 1H-pyrrole-2-carbonitrile according to the general procedure A (−25 °C, CH_3NO_2 , 45 min). Purification by flash chromatography on silica gel with 20:1 hexanes-EtOAc for elution gave the title compound as colorless syrup (98 mg, 48%).

R_f 0.52 (25% EtOAc/hexanes);

^1H NMR (400 MHz, CDCl_3) δ 12.06 (s, br, 1H), 8.34 (s, br, 1H), 6.85 (dd, $J = 4.0, 2.4$ Hz, 1H), 6.42 (d, $J = 1.2$ Hz, 1H), 6.37 (dd, $J = 3.2, 2.4$ Hz, 1H), 6.25 (dd, $J = 6.0, 2.4$ Hz, 1H), 4.33 (q, $J = 7.2$ Hz, 2H), 2.25 (s, 3H), 1.39 (t, $J = 7.2$ Hz, 3H);

^{13}C NMR (100 MHz, CDCl_3) δ 167.9, 132.1, 124.3, 121.9, 118.3, 115.8, 108.9, 108.3, 104.7, 60.2, 14.3, 13.6;

HRMS m/z calcd for $\text{C}_{12}\text{H}_{15}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 219.1134, found: 219.1130.

2-(1*H*-Pyrrol-2-yl)-4,5,6,7-tetrahydro-1*H*-indole-3-carboxylic acid ethyl ester (table 1, entry 8)

The title compound was prepared from the corresponding cyclopropane and 1*H*-pyrrole-2-carbonitrile according to the general procedure A (−10 °C, CH₃NO₂, 45 min). Purification by flash chromatography on silica gel with 15:1 hexanes-EtOAc for elution gave the title compound as colorless syrup (162 mg, 62%).

*R*_f 0.68 (25% EtOAc/hexanes);

IR (thin film) ν 3420-3180, 1660 cm^{−1};

¹H NMR (400 MHz, CDCl₃) δ 12.09 (s, br, 1H), 8.14 (s, br, 1H), 6.82 (dd, *J* = 2.0, 2.0 Hz, 1H), 6.33 (dd, *J* = 2.0, 2.0 Hz, 1H), 6.22 (dd, *J* = 4.0, 2.4 Hz, 1H), 4.29 (q, *J* = 7.2 Hz, 2H), 2.70 (t, *J* = 5.6 Hz, 2H), 2.53 (t, *J* = 6.4 Hz, 2H), 1.81-1.71 (m, 4H), 1.36 (t, *J* = 7.2 Hz, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 168.0, 130.3, 126.8, 124.6, 119.2, 118.2, 108.8, 107.2, 104.2, 60.0, 23.9, 23.5, 22.6, 22.5, 14.4;

HRMS *m/z* calcd for C₁₅H₁₉N₂O₂ [M+H]⁺ 259.1447, found: 259.1449.

2-(3,4-Diethyl-1*H*-pyrrol-2-yl)-4,5,6,7-tetrahydro-1*H*-indole-3-carboxylic acid ethyl ester (table 1, entry 9)

The title compound was prepared from the corresponding cyclopropane and 3,4-diethyl-1*H*-pyrrole-2-carbonitrile according to the general procedure A (−35 °C, C₂H₅NO₂, 45 min). Purification by flash chromatography on silica gel with 15:1 hexanes-EtOAc for elution gave the title compound as colorless syrup (171 mg, 82%).

*R*_f 0.68 (25% EtOAc/hexanes);

IR (thin film) ν 3520-3180, 1665 cm^{−1};

¹H NMR (400 MHz, CDCl₃) δ 11.56 (s, br, 1H), 8.13 (s, br, 1H), 6.60 (s, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 2.75-2.69 (m, 2H), 2.68 (dq, *J* = 2.0, 7.6, Hz, 2H), 2.58-2.54 (m, 2H), 2.49 (dq, *J* = 2.0, 7.6 Hz, 2H), 1.85-1.72 (m, 4H), 1.35 (td, *J* = 7.2, 2.0 Hz, 3H), 1.23 (t, *J* = 7.6 Hz, 6H);

¹³C NMR (100 MHz, CDCl₃) δ 167.8, 130.9, 126.3, 125.5, 120.9, 120.0, 118.9, 114.5, 107.9, 59.8, 23.9, 23.5, 22.7, 22.6, 18.6, 18.2, 15.6, 14.8, 14.4;

HRMS *m/z* calcd for C₁₉H₂₇N₂O₂ [M+H]⁺ 315.2073, found: 315.2078.

4-(3-Hydroxy-propyl)-1H-1'H-[2,2']bipyrrolyl-3-carboxylic acid ethyl ester (table 1, entry 10)

The title compound was prepared from the corresponding cyclopropane and 1H-pyrrole-2-carbonitrile according to the general procedure A (−10 °C, CH₃NO₂, 25 min). Purification by flash chromatography on silica gel with 5:1 hexanes-EtOAc for elution gave the title compound as colorless solid (231 mg, 46%).

R_f 0.28 (50% EtOAc/hexanes);

¹H NMR (400 MHz, CDCl₃) δ 11.94 (s, br, 1H), 8.51 (s, br, 1H), 6.84 (t, *J* = 1.2 Hz, 1H), 6.44 (s, 1H), 6.38 (d, *J* = 2.0 Hz, 1H), 6.25-6.23 (m, 1H), 4.32 (qd, *J* = 7.2, 2.0 Hz, 2H), 3.68 (td, *J* = 6.8, 2.0 Hz, 2H), 2.75 (t, *J* = 7.6 Hz, 2H), 1.84 (dq, *J* = 6.8, 6.8 Hz, 2H), 1.53 (s, br, 1H), 1.37 (td, *J* = 7.2, 1.6 Hz, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 167.6, 132.4, 125.8, 124.2, 118.4, 115.6, 109.0, 107.6, 105.1, 62.6, 60.3, 33.4, 23.7, 14.3;

HRMS *m/z* calcd for C₁₄H₁₉N₂O₂ [M+H]⁺ 263.1396, found: 263.1392.

3',4'-Diethyl-4-(3-hydroxy-propyl)-1H-1'H-[2,2']bipyrrolyl-3-carboxylic acid ethyl ester (table 1, entry 11)

The title compound was prepared from the corresponding cyclopropane and 3,4-diethyl-1H-pyrrole-2-carbonitrile according to the general procedure A (−30 °C, C₂H₅NO₂, 45 min). Purification by flash chromatography on silica gel with 3:1 hexanes-EtOAc for elution gave the title compound as colorless solid (76 mg, 54%).

R_f 0.28 (50% EtOAc/hexanes);

IR (thin film) ν 3580-3250, 1726 cm^{−1};

¹H NMR (400 MHz, CDCl₃) δ 11.06 (s, br, 1H), 8.41 (s, br, 1H), 6.60 (d, *J* = 2.4 Hz, 1H), 6.51 (d, *J* = 2.4 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 3.67 (q, *J* = 6.4 Hz, 2H), 2.77 (q, *J* = 7.6 Hz, 2H), 2.63 (q, *J* = 7.6 Hz, 2H), 2.48 (q, *J* = 7.2 Hz, 2H), 1.88-1.81 (m, 3H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.21 (t, *J* = 7.6 Hz, 3H), 1.19 (t, *J* = 7.6 Hz, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 167.4, 132.5, 125.64, 125.57, 121.7, 119.7, 115.3, 114.7, 108.8, 62.5, 60.1, 33.5, 23.5, 18.4, 18.1, 15.8, 14.7, 14.2;

HRMS *m/z* calcd for C₁₈H₂₇N₂O₃ [M+H]⁺ 319.2022, found: 319.2019.

3',4'-Diethyl-4-(2-hydroxy-ethyl)-5-methyl-1H-1'H-[2,2']bipyrrolyl-3-carboxylic acid ethyl ester (table 1, entry 12)

The title compound was prepared from the corresponding cyclopropane and 3,4-diethyl-1H-pyrrole-2-carbonitrile according to the general procedure A (−25 °C, CH₃NO₂, 1.0 h). Purification by flash chromatography on silica gel with 3:1 hexanes-EtOAc for elution gave the title compound as colorless solid (151 mg, 84%).

R_f 0.31 (50% EtOAc/hexanes);

IR (thin film) ν 3500–3150, 1670 cm^{−1};

¹H NMR (400 MHz, CDCl₃) δ 10.82 (s, br, 1H), 8.20 (s, br, 1H), 6.57 (d, *J* = 2.7 Hz, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 3.74 (t, *J* = 6.4 Hz, 2H), 2.90 (t, *J* = 7.0 Hz, 2H), 2.61 (t, *J* = 7.6 Hz, 2H), 2.47 (t, *J* = 7.6 Hz, 2H), 2.21 (s, 3H), 2.05 (s, br, 1H), 1.31 (t, *J* = 7.2 Hz, 3H), 1.20 (t, *J* = 7.6 Hz, 3H), 1.18 (t, *J* = 7.6 Hz, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 167.1, 130.5, 125.5, 124.9, 121.5, 119.6, 116.6, 114.5, 109.3, 63.4, 60.0, 29.1, 18.4, 18.1, 15.7, 14.7, 14.1, 11.0;

HRMS *m/z* calcd for C₁₈H₂₇N₂O₂ [M+H]⁺ 319.2022, found: 319.2025.

3',4'-Diethyl-4-(2-hydroxy-ethyl)-1H-1'H-[2,2']bipyrrolyl-3-carboxylic acid ethyl ester (table 1, entry 13)

The title compound was prepared from the corresponding cyclopropane and 3,4-diethyl-1H-pyrrole-2-carbonitrile according to the general procedure A (−40 °C, C₂H₅NO₂, 1.0 h). Purification by flash chromatography on silica gel with 3:1 hexanes-EtOAc for elution gave the title compound as colorless solid (86 mg, 42%).

R_f 0.45 (50% EtOAc/hexanes);

¹H NMR (400 MHz, CDCl₃) δ 11.13 (s, br, 1H), 8.41 (s, br, 1H), 6.609 (s, 1H), 6.607 (s, 1H), 4.27 (dq, *J* = 2.0, 7.2 Hz, 2H), 3.81 (t, *J* = 6.2 Hz, 2H), 2.97 (dt, *J* = 2.0, 6.2 Hz, 2H), 2.63 (tq, *J* = 2.0, 7.6 Hz, 2H), 2.47 (dt, *J* = 2.0, 7.6 Hz, 2H), 1.33 (dt, *J* = 2.0, 7.6 Hz, 3H), 1.24–1.17 (m, 6H);

¹³C NMR (100 MHz, CDCl₃) δ 167.2, 133.1, 125.7, 122.0, 121.9, 119.5, 116.4, 114.9, 108.8, 63.0, 60.2, 30.9, 18.5, 18.1, 15.8, 14.8, 14.2;

HRMS *m/z* calcd for C₁₇H₂₅N₂O₃ [M+H]⁺ 305.1865, found: 305.1861.

2-Thiophen-2-yl-1H-3-carboxylic acid ethyl ester (table 2, entry 1)

The title compound was prepared from the corresponding cyclopropane and 2-thiophenecarbonitrile according to the general procedure B (−30 °C, C₂H₅NO₂, 3.5 h).

Purification by flash chromatography on silica gel with 5:1 hexanes-EtOAc for elution gave the title compound as colorless syrup (136 mg, 47%).

R_f 0.51 (33% EtOAc/hexanes);

^1H NMR (400 MHz, CDCl_3) δ 8.56 (s, br, 1H), 7.50 (dd, J = 2.0, 1.2 Hz, 1H), 7.31 (dd, J = 5.0, 1.0 Hz, 1H), 7.05 (dd, J = 5.2, 4.0 Hz, 1H), 6.72-6.70 (m, 2H), 4.25 (q, J = 7.2 Hz, 2H), 1.30 (t, J = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, CDCl_3) δ 164.7, 133.0, 130.1, 127.2, 127.1, 125.9, 117.8, 112.6, 112.4, 59.8, 14.4;

HRMS m/z calcd for $\text{C}_{11}\text{H}_{12}\text{NO}_2\text{S}$ $[\text{M}+\text{H}]^+$ 222.0589, found: 222.0583.

5-Methyl-2-thiophen-2-yl-1H-3-carboxylic acid ethyl ester (table 2, entry 2)

The title compound was prepared from the corresponding cyclopropane and 2-thiophenecarbonitrile according to the general procedure B ($-15\text{ }^\circ\text{C}$, CH_3NO_2 , 3.0 h). Purification by flash chromatography on silica gel with 10:1 hexanes-EtOAc for elution gave the title compound as colorless syrup (114 mg, 69%).

R_f 0.46 (25% EtOAc/hexanes);

IR (thin film) ν 3390-3240, 1675 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 8.39 (s, br, 1H), 7.46 (dd, J = 3.3, 1.0 Hz, 1H), 7.27 (dd, J = 4.8, 1.0 Hz, 1H), 7.02 (dd, J = 5.2, 4.0 Hz, 1H), 6.36 (dd, J = 1.0, 1.0 Hz, 1H), 4.23 (q, J = 7.2 Hz, 2H), 2.25 (s, 3H), 1.29 (t, J = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, CDCl_3) δ 164.8, 133.4, 129.0, 127.9, 127.1, 126.7, 125.4, 112.5, 109.8, 59.7, 14.4, 12.7;

HRMS m/z calcd for $\text{C}_{12}\text{H}_{14}\text{NO}_2\text{S}$ $[\text{M}+\text{H}]^+$ 236.0745, found: 236.0743.

4-Methyl-2-thiophen-2-yl-1H-3-carboxylic acid ethyl ester (table 2, entry 3)

The title compound was prepared from the corresponding cyclopropane and 2-thiophenecarbonitrile according to the general procedure B ($-25\text{ }^\circ\text{C}$, CH_3NO_2 , 3.0h). Purification by flash chromatography on silica gel with 10:1 hexanes-EtOAc for elution gave the title compound as colorless syrup (119 mg, 63%).

R_f 0.37 (25% EtOAc/hexanes);

^1H NMR (400 MHz, CDCl_3) δ 8.25 (s, br, 1H), 7.34 (d, J = 1.2 Hz, 1H), 7.30 (d, J = 5.2, Hz, 1H), 7.03 (dd, J = 5.2, 4.0 Hz, 1H), 6.54 (dd, J = 1.6, 0.8 Hz, 1H), 4.23 (q, J = 7.2 Hz, 2H), 2.27 (s, 3H), 1.27 (t, J = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, CDCl_3) δ 165.4, 133.8, 130.3, 127.1, 127.0, 126.8, 122.8, 116.9, 109.7, 59.6, 14.3, 12.7;

HRMS m/z calcd for $\text{C}_{12}\text{H}_{14}\text{NO}_2\text{S}$ $[\text{M}+\text{H}]^+$ 236.0745, found: 236.0753.

2-Thiophen-2-yl-4,5,6,7-tetrahydro-1H-indole-3-carboxylic acid ethyl ester (table 2, entry 4)

The title compound was prepared from the corresponding cyclopropane and 2-thiophenecarbonitrile according to the general procedure B (−25 °C, CH₃NO₂, 1.5 h). Purification by flash chromatography on silica gel with 10:1 hexanes-EtOAc for elution gave the title compound as colorless syrup (83 mg, 37%).

R_f 0.52 (25% EtOAc/hexanes);

IR (thin film) ν 3650-3150, 1650 cm^{−1};

¹H NMR (400 MHz, CDCl₃) δ 8.14 (s, br, 1H), 7.36 (dd, *J* = 3.6, 0.8 Hz, 1H), 7.25 (dt, *J* = 0.8, 5.2 Hz, 1H), 7.01 (dd, *J* = 5.2, 3.6 Hz, 1H), 4.23 (q, *J* = 7.2 Hz, 2H), 2.72 (t, *J* = 6.0 Hz, 2H), 2.53 (t, *J* = 6.0 Hz, 2H), 1.80-1.73 (m, 4H), 1.27 (t, *J* = 7.2 Hz, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 165.4, 134.0, 128.5, 128.1, 127.0, 126.7, 125.3, 120.4, 110.8, 59.4, 30.9, 23.4, 22.7, 22.5, 14.3;

HRMS *m/z* calcd for C₁₅H₁₈NO₂S [M+H]⁺ 276.1058, found: 276.1052.

4-(2-Hydroxy-ethyl)-2-thiophen-2-yl-1H-3-carboxylic acid ethyl ester (table 2, entry 5)

The title compound was prepared from the corresponding cyclopropane and 2-thiophenecarbonitrile according to the general procedure B (−40 °C, C₂H₅NO₂, 4.0 h). Purification by flash chromatography on silica gel with 3:1 hexanes-EtOAc for elution gave the title compound as colorless solid (114 mg, 41%). R_f 0.31 (50% EtOAc/hexanes); ¹H NMR (400 MHz, CDCl₃) δ 8.72 (s, br, 1H), 7.31 (d, *J* = 4.8 Hz, 1H), 7.26 (d, *J* = 3.6 Hz, 1H), 7.02 (dd, *J* = 4.8, 3.6 Hz, 1H), 6.61 (d, *J* = 2.4 Hz, 1H), 4.21 (q, *J* = 7.2 Hz, 2H), 3.81 (t, *J* = 6.0 Hz, 2H), 2.96 (t, *J* = 6.0 Hz, 2H), 2.45 (s, br, 1H), 1.22 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 165.7, 133.6, 130.5, 127.4, 126.8, 126.1, 123.7, 117.8, 111.7, 63.5, 59.9, 29.9, 14.1; HRMS *m/z* calcd for C₁₃H₁₆NO₃ [M+H]⁺ 266.0851, found: 266.0851. Purification by flash chromatography on silica gel was unable to bring this compound up to acceptable purity, therefore it was carried on through the decarboxylation procedure.

4-(3-Hydroxy-propyl)-2-thiophen-2-yl-1H-3-carboxylic acid ethyl ester (table 2, entry 6)

The title compound was prepared from the corresponding cyclopropane and 2-thiophenecarbonitrile according to the general procedure B (−30 °C, C₂H₅NO₂, 2.5 h). Purification by flash chromatography on silica gel with 3:1 hexanes-EtOAc for elution gave the title compound as colorless solid (187 mg, 73%). R_f 0.25 (50% EtOAc/hexanes); IR (thin film) ν

3620-3175, 1665 cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 8.92 (s, br, 1H), 7.31-7.25 (m, 2H), 7.03-7.01 (m, 2H), 6.55 (s, 1H), 4.20 (q, $J = 7.2$ Hz, 2H), 3.65-3.63 (m, 2H), 2.79 (q, $J = 7.6$ Hz, 2H), 2.54 (s, br, 1H), 1.83-1.82 (m, 2H), 1.23 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 165.7, 133.8, 130.1, 127.2, 126.8, 126.7, 125.9, 116.9, 111.5, 61.8, 59.8, 33.7, 22.3, 14.1; HRMS m/z calcd for $\text{C}_{14}\text{H}_{18}\text{NO}_3\text{S}$ $[\text{M}+\text{H}]^+$ 280.1007, found: 280.0997. Purification by flash chromatography on silica gel was unable to bring this compound up to acceptable purity, therefore it was carried on through the decarboxylation procedure.

5-Methyl-1H, 1'H-[2,2']bipyrrole

To a solution of the bipyrrole product (table 1, entry 1, 143 mg, 0.65 mmol) in ethylene glycol (6.0 mL) was added powdered NaOH (260 mg, 6.5 mmol). After stirring at 160 °C for 5 min, the reaction mixture was treated with 10% aqueous NaCl (15 mL) and the resulting solution was extracted with CH_2Cl_2 (3×10 mL). The combined organic extracts were washed with H_2O (8 mL), brine (6 mL) and dried (MgSO_4). After filtration through a small pad of celite, volatiles were removed under reduced pressure. Purification by flash chromatography on silica gel with 20:1 hexanes-EtOAc for elution gave the title compound as a white solid (88 mg, 92%).²

R_f 0.52 (25% EtOAc/hexanes);

^1H NMR (400 MHz, CDCl_3) δ 8.12 (s, br, 1H), 7.88 (s, br, 1H), 6.72 (dd, $J = 4.0, 2.8$ Hz, 1H), 6.22 (dd, $J = 6.4, 2.4$ Hz, 1H), 6.15 (dt, $J = 4.4, 1.6$ Hz, 1H), 6.06 (t, $J = 2.8$ Hz, 1H), 5.90-5.88 (m, 1H), 2.28 (s, 3H);

^{13}C NMR (100 MHz, CDCl_3) δ 127.7, 126.2, 124.5, 117.2, 109.2, 107.0, 103.6, 102.9, 13.0;

HRMS m/z calcd for $\text{C}_9\text{H}_{11}\text{N}_2$ $[\text{M}+\text{H}]^+$ 147.0922, found: 147.0918.

2-Thiophen-2-yl-1H-pyrrole

The title compound was prepared from the thienylpyrrole product (table 2, entry 1) according to the decarboxylation procedure described above. Purification by flash chromatography on silica gel with 15:1 hexanes-EtOAc for elution gave the title compound as colorless solid (81 mg, 96%).³

R_f 0.41 (33% EtOAc/hexanes);

^1H NMR (400 MHz, CDCl_3) δ 8.28 (s, br, 1H), 7.13 (dt, $J = 8.0, 3.2$ Hz, 1H), 7.02-6.99 (m, 2H), 6.79 (dt, $J = 8.4, 1.6$ Hz, 1H), 6.41-6.39 (m, 1H), 6.25 (dt, $J = 6.0, 2.8$ Hz, 1H);

^{13}C NMR (100 MHz, CDCl_3) δ 136.2, 127.6, 122.7, 120.9, 118.5, 110.0, 109.7, 106.7;

HRMS m/z calcd for $\text{C}_8\text{H}_8\text{NS}$ $[\text{M}+\text{H}]^+$ 150.0377, found: 150.0378.

² Rapoport, H; Bordner, J. *J. Org. Chem.* **29**, 2727-2731.

³ Munno, G. D.; Lucchesini, F.; Neidlein, R. *Tetrahedron* **1993**, 49, 6863-6872.

2-(5-Thiophen-2-yl-1H-pyrrol-3-yl)-ethanol

The title compound was prepared from the thienylpyrrole product (table 2, entry 5) according to the decarboxylation procedure described above, expect that the reaction time was 2 min. Purification by flash chromatography on silica gel with 2:1 hexanes-EtOAc for elution gave the title compound as colorless solid (62 mg, 81%).

R_f 0.52 (66% EtOAc/hexanes);

^1H NMR (400 MHz, CDCl_3) δ 8.17 (s, br, 1H), 7.12 (dd, $J = 3.6, 2.4$ Hz, 1H), 6.99 (s, 1H), 6.98 (d, $J = 0.8$ Hz, 1H), 6.65 (dd, $J = 2.4, 1.6$ Hz, 1H), 6.62 (t, $J = 2.4$ Hz, 1H), 3.79 (t, $J = 6.4$ Hz, 2H), 2.73 (t, $J = 6.4$ Hz, 2H), 1.57 (s, br, 1H);

^{13}C NMR (100 MHz, CDCl_3) δ 136.1, 127.6, 127.1, 122.7, 121.5, 120.8, 116.9, 107.1, 63.3, 30.4;

HRMS m/z calcd for $\text{C}_{10}\text{H}_{12}\text{NS}$ $[\text{M}+\text{H}]^+$ 194.0644, found: 194.0640.

3-(5-Thiophen-2-yl-1H-pyrrol-3-yl)-propan-1-ol

The title compound was prepared from the thienylpyrrole product (table 2, entry 6) according to the decarboxylation procedure described above, expect that the reaction time was 2 min. Purification by flash chromatography on silica gel with 2:1 hexanes-EtOAc for elution gave the title compound as colorless solid (86 mg, 87%).

R_f 0.52 (66% EtOAc/hexanes);

^1H NMR (400 MHz, CDCl_3) δ 8.16 (s, br, 1H), 7.10 (t, $J = 3.2$ Hz, 1H), 6.98 (d, $J = 0.4$ Hz, 1H), 6.97 (s, 1H), 6.57 (s, 1H), 6.27 (t, $J = 2.0$ Hz, 1H), 3.70 (t, $J = 6.4$ Hz, 2H), 2.56 (t, $J = 7.6$ Hz, 2H), 1.86 (tt, $J = 6.4, 6.4$ Hz, 2H), 1.40 (s, br, 1H);

^{13}C NMR (100 MHz, CDCl_3) δ 136.3, 127.6, 126.7, 125.2, 122.5, 120.6, 115.9, 106.9, 62.7, 33.7, 23.2;

HRMS m/z calcd for $\text{C}_{11}\text{H}_{14}\text{NS}$ $[\text{M}+\text{H}]^+$ 208.0796, found: 208.0802.