

Efficient Synthesis of an Enantiopure Thiasteroid by a Double Heck Reaction

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Supporting Information: Experimental procedures with NMR assignments for the compounds **8a-8c** and **10**.

3-Bromo-2-(2,2-dibromo-vinyl)-thiophene (10) : A solution of PPh₃ (62.5 g, 238 mmol) in CH₂Cl₂ (238 mL) was cooled under an atmosphere of argon to 0 °C. After this, a solution of CBr₄ (39.5 g, 119 mmol) in CH₂Cl₂ (238 mL) was added and the mixture was allowed to warm to room temperature over 30 min. A solution of aldehyde **9a** (11.4 g, 59.6 mmol) in CH₂Cl₂ (238 mL) was then added and stirring was continued at room temperature for 2 h. The reaction mixture was subsequently poured into pentane (400 mL), filtered, and concentrated in vacuo. Purification by column chromatography provided **10** (17.5 g, 50.4 mmol, 85%) as yellow oil: *R*_f = 0.71 (pentane). – UV (CH₃CN): λ_{max} (lg ε) = 297.0 nm (4.2696). – IR (KBr): $\tilde{\nu}$ = 3101 cm⁻¹ (C-H), 3089 (C-H), 1477 (C=C), 882 (Ar-H), 714 (C=C). – ¹H NMR (200 MHz, CDCl₃): δ = 7.03 (d, *J* = 5.0 Hz, 1 H, 4-H), 7.40 (d, *J* = 5.0 Hz, 1 H, 5-H), 7.80 (s, 1 H, 1'-H). – ¹³C NMR (50.3 MHz, CDCl₃): δ = 89.3 (C-2'), 114.2 (C-3), 126.9 (C-4), 129.7, 129.7 (C-1', C-5), 132.5 (C-2). – EI-MS (70 eV): *m/z* (%) = 345.8 (100) [M⁺], 266.8 (24) [M⁺ - Br], 187.9 (72) [M⁺ - Br - Br], 45.0 (15) [CHS⁺]. – EI-HRMS (C₆H₃Br₃S): calcd. 343.7506; found: 343.7506.

(Z)-3-Bromo-2-(2-bromo-vinyl)-thiophene (8a) : A degassed solution of **10** (4.12 g, 11.9 mmol) in anhydrous toluene (60 mL) and Pd(PPh₃)₄ (0.27 g, 2.0 mol %) was treated with *n*Bu₃SnH (3.81 g, 13.1 mmol, 3.47 mL) and the mixture was stirred for 3 h at room temperature. The reaction mixture was poured into pentane (60 mL), washed with water (3 × 50 mL), brine (50 mL), and dried over MgSO₄. Concentration in vacuo and purification by column chromatography provided **8a** (2.89 g, 10.7 mmol, 91%) as yellow oil: *R*_f = 0.66 (pentane/*tert*butyl methyl ether 1:100). – UV (CH₃CN): λ_{max} (lg ε) = 196.0 (4.063), 204.5 (4.072), 285.5 (4.161). – IR (KBr): $\tilde{\nu}$ = 3106 cm⁻¹ (C-H), 3084 (C-H), 1077 (Ar-Br), 875 (Ar-H), 699 (*cis*-C=C-H). – ¹H NMR (200 MHz, CDCl₃): δ = 6.47 (d, *J* = 8.0 Hz, 1 H, 2'-H), 7.05 (d, *J* = 5.4 Hz, 1 H, 4-H), 7.40 (d, *J* = 5.4 Hz, 1 H, 5-H), 7.46 (d, *J* = 8.0 Hz, 1 H, 1'-H). – ¹³C NMR (50.3 MHz, CDCl₃): δ = 106.4 (C-2'), 114.3 (C-3), 125.0 (C-4), 126.7 (C-1'), 129.5 (C-5), 132.7 (C-2). – EI-MS (70 eV): *m/z* (%) = 267.8 (100) [M⁺], 188.9 (44) [M⁺ - Br], 108.0 (66) [M⁺ - Br - Br]. – C₆H₄Br₂S (268.0).

(Z)-3-Bromo-2-(2-iodo-vinyl)-thiophene (8b) : To a suspension of Iodine-methylenephosphoniumiodide (3.47 g, 6.55 mmol) in THF (38 mL) was added dropwise KHMDS (6.75 mmol, 13.5 mL of a 0.5 M solution in toluene) at room temperature and the reaction mixture was stirred for 3 min. The resulting mixture was cooled to -78 °C and a solution of aldehyde **9a** (1.00 g, 5.25 mmol) in THF (15 mL) was added. After stirring for 15 min at -78 °C and a further 30 min at room temperature, the ensuing mixture was quenched with saturated aqueous NH₄Cl (10 mL). The organic layer was washed with water (2 × 20 mL) and brine (20 mL), dried (Na₂SO₄) and concentrated in vacuo. Purification by column chromatography afforded **8b** (1.47 g, 4.65 mmol, 89%, *Z/E* = 6 : 1): *R*_f = 0.67 (pentane). – ¹H NMR (200 MHz, CDCl₃): δ = 6.63 (d, *J* = 8.0 Hz, 1 H, 2'-H), 7.07 (d, *J* = 5.0 Hz, 1 H, 4-H), 7.39 (d, *J* = 5.0 Hz, 1 H, 5-H), 7.74 (d, *J* = 8.0 Hz, 1 H, 1'-H). – ¹³C NMR (50.3 MHz, CDCl₃): δ = 78.7 (C-2'), 115.0 (C-3), 125.7 (C-4), 129.8 (C-5), 131.3 (C-1'), 134.1 (C-2). – EI-MS (70 eV): *m/z* (%) = 314.1 (100) [M⁺], 236.2 (8) [M⁺ - Br], 189.1 (55) [M⁺ - I], 127.1 (2) [I⁺], 108.1 (55) [M⁺ - Br - I], 82.0 (5) [HBr⁺], 45.1 [CHS⁺]. – C₆H₄BrIS (314.2).

(Z)-3-Iodo-2-(2-iodo-vinyl)-thiophene (8c) : To a suspension of Iodine-methylenphosphoniumiodide (6.46 g, 10.9 mmol) in THF (35 mL) was added dropwise KHMDS (10.9 mmol, 14.6 mL of a 0.75 M solution in toluene) at room temperature and stirred for 15 min. The resulting mixture was cooled to $-78\text{ }^{\circ}\text{C}$ and a solution of aldehyde **9b** (2.00 g, 8.40 mmol) in THF (35 mL) was added. After stirring for 4 h at $-78\text{ }^{\circ}\text{C}$ and a further 30 min at room temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl (10 mL). The organic layer was washed with water ($2 \times 20\text{ mL}$) and brine (20 mL), dried (Na_2SO_4) and concentrated in vacuo. Purification by column chromatography afforded **8c** (1.55 g, 4.28 mmol, 51%): $R_f = 0.75$ (pentane/*tert*butyl methyl ether 10:1). – UV (CH_3CN): λ_{max} ($\lg \epsilon$) = 288.0 nm (4.149), 299.0 (4.182). – IR (KBr): $\tilde{\nu} = 3100\text{ cm}^{-1}$ (C-H), 3062 (C-H), 1299 (Ar-H), 863 (Ar-H), 698 (*cis*-C=C-H). – ^1H NMR (200 MHz, CDCl_3): $\delta = 6.66$ (d, $J = 8.7\text{ Hz}$, 1 H, 2'-H), 7.18 (d, $J = 4.8\text{ Hz}$, 1 H, 4-H), 7.39 (d, $J = 4.8\text{ Hz}$, 1 H, 5-H), 7.69 (d, $J = 8.7\text{ Hz}$, 1 H, 1'-H). – ^{13}C NMR (50.3 MHz, CDCl_3): $\delta = 79.2$ (C-2'), 87.2 (C-3), 126.8 (C-1'), 134.2 (C-4), 134.7 (C-5), 137.3 (C-2). – EI-MS (70 eV): m/z (%) = 361.7 (81) [M^+], 234.8 (100) [$\text{M}^+ - \text{I}$], 126.9 (11) [I^+], 108.0 (44) [$\text{M}^+ - \text{I} - \text{I}$], 45.0 (7) [CHS^+]. – EI-HRMS ($\text{C}_6\text{H}_4\text{I}_2\text{S}$): calcd. 361.8123; found: 361.8123.