Manuscript Title:

Transition-metal Free Method for Synthesis of Benzo[b]thiophene from o-Halo-vinylbenzenes and K$_2$S via Direct S$_{2}$Ar-type Reaction, Cyclization, and Dehydrogenation Process

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1) General Information

The $^1$H and $^{13}$C NMR spectra were recorded on a spectrometer operating at 500 MHz and 125 MHz, respectively. The $^1$H NMR spectra were taken in CDCl$_3$ and the chemical shifts are given in ppm with respect to tetramethylsilane (TMS) used as an internal standard. The $^{13}$C NMR spectra were taken in CDCl$_3$ and the central peak of the solvent was adjusted to 77.00 ppm and used as a reference. All reagents were used directly as obtained commercially unless otherwise noted.

2) Synthesis of Starting Materials

Preparation of Starting Materials 1

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\begin{align*}
\text{R}^1 & \text{C} & \text{F} & \text{Br} & \text{PPh}_3 & \text{toluene} & \text{R}^1 & \text{C} & \text{F} & \text{Br} & \text{PPh}_3 & \text{KO}^\text{Bu}, \text{THF} & \text{R}^2 & \text{CHO} & \text{R}^2 & \text{C} & \text{R}^2 & \text{F} \\
\end{align*}
\]

**Step 1  Preparation of (2-fluorobenzyl)triphenylphosphonium bromide derivatives:**

A solution of 2-fluorobenzyl bromide (1.25 g, 5 mmol) and PPh$_3$ (1.965 g, 7.5 mmol) in toluene (150 mL) was heated at 120 °C for 6 h, then cooled to room temperature. The resulting precipitate was collected by filtration, washed with toluene (50 mL) and dried in vacuo to give the product (2.381g, 4.65 mmol, 93%) as a white solid.

**Step 2  Preparation of 1-fluoro-2-styrylbenzene derivatives:**

(2-Fluorobenzyl)triphenylphosphonium bromide (2.4 mmol, 1.2 equiv) was dissolved in THF (10 mL) and potassium tert-butoxide (2.8 mmol, 1.4 equiv) was added at 0 °C to give a cloudy orange suspension. After 30 minutes, aldehyde (2 mmol) in THF (5 mL) was added via cannula, and the suspension turned a yellow colour. The reaction was left to gradually warm to room temperature, until complete consumption of starting material was indicated by TLC (about 5-12 h). The mixture was quenched with water and the organic layer extracted with ethyl acetate (3 x 50 mL). The combined extracts were washed with brine (1 x 100 mL), dried (MgSO$_4$), concentrated in vacuo and purified by column chromatography to product as a colourless liquid.
3) Typical Procedures

**General Procedure for Preparation of Benzo[b]thiophenes:**

An oven-dried Schlenk tube was charged with K$_2$S (0.9 mmol, 3 equiv) and 1-fluoro-2-styryl derivatives (0.3 mmol). The tube was evacuated and backfilled with nitrogen before DMF or CH$_3$CN (2 mL) were added. The reaction mixture was stirred at 140 °C, and after 24 hours was quenched with water. The mixture extracted with ethyl acetate, and the combined organic layers were washed with H$_2$O and brine, dried over Na$_2$SO$_4$, concentrated in vacuo and purified by column chromatography to afford a white solid.

**One-Pot Synthesis of Benzothiophenes:**

(2-Fluorobenzyl)triphenylphosphonium bromide (0.36 mmol, 1.2 equiv) was dissolved in THF (3 mL) and potassium tert-butoxide (0.42 mmol, 1.4 equiv) was added at 0 °C to give a cloudy orange suspension in a Schlenk tube. After 30 minutes, aldehyde (0.3 mmol) in THF (1 mL) was added via cannula, and the suspension turned a yellow colour. After 5h, K$_2$S (0.9 mmol, 3 equiv) and DMF (2 mL) was added to the mixture. The reaction mixture was stirred at 140 °C for 24 h. The mixture extracted with ethyl acetate, and the combined organic layers were washed with H$_2$O and brine, dried over Na$_2$SO$_4$, concentrated in vacuo and purified by column chromatography (SiO$_2$, hexanes) to afford a white solid (50.4 mg, 80%).

**Preparation of Benzo[b]thiophenes via Added Extra D$_2$O:**

An oven-dried Schlenk tube was charged with K$_2$S (0.9 mmol, 3 equiv), 1-fluoro-2-styryl derivatives (0.3 mmol) and D$_2$O (3 equiv). The tube was evacuated
and backfilled with nitrogen before DMF (2 mL) were added. The reaction mixture was stirred at 140 °C, and after 24 hours was quenched with water. The mixture extracted with ethyl acetate, and the combined organic layers were washed with H₂O and brine, dried over Na₂SO₄, concentrated in vacuo and purified by column chromatography to afford a white solid (compound C, 57 mg, 92%).

4) Procedures and Characterization Data:

![Chemical Structure](image1)

2-phenylbenzo[b]thiophene (2a): The product was purified by flash chromatography to give 60 mg (96%) as a yellow solid. \(^1\)H NMR (CDCl₃, 500 MHz) δ = 7.82 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 7.5 Hz, 1H), 7.72 (d, J = 8.5 Hz, 2H), 7.54 (s, 1H), 7.42 (t, J = 7.8 Hz, 2H), 7.36-7.29 (m, 3H). \(^13\)C NMR (CDCl₃, 125 MHz) δ = 144.2, 140.7, 139.5, 134.3, 128.9, 128.2, 126.5, 124.3, 123.5, 122.2, 119.4.

![Chemical Structure](image2)

2-(p-tolyl)benzo[b]thiophene (2b): The product was purified by flash chromatography to give 62 mg (92%) as a white solid. \(^1\)H NMR (CDCl₃, 500 MHz) δ = 7.80 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 7.5 Hz, 1H), 7.60 (d, J = 8.0 Hz, 2H), 7.48 (s, 1H), 7.34-7.27 (m, 2H), 7.22 (d, J = 8.0 Hz, 2H), 2.38 (s, 3H). \(^13\)C NMR (CDCl₃, 125 MHz) δ = 144.4, 140.8, 139.3, 138.2, 131.5, 129.6, 126.4, 124.4, 124.1, 123.4, 122.2, 118.8, 21.2.

![Chemical Structure](image3)

2-(4-methoxyphenyl)benzo[b]thiophene (2c): The product was purified by flash chromatography to give 60 mg (84%) as a white solid. \(^1\)H NMR (CDCl₃, 500 MHz) δ = 7.80 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 7.5 Hz, 1H), 7.65-7.63 (m, 2H), 7.42 (s, 1H), 7.35-7.31 (m, 1H), 7.29-7.26 (s, 1H), 6.70-6.94 (m, 2H), 3.85 (s, 3H). \(^13\)C NMR (CDCl₃, 125 MHz) δ = 159.8, 144.1, 140.9, 139.2, 127.7, 127.0, 124.4, 123.9, 123.2, 122.2, 118.2, 114.3, 55.4.
2-(3-methoxyphenyl)benzo[b]thiophene (2d): The product was purified by flash chromatography to give 63 mg (88%) as a white solid. \( ^1H \text{NMR} (\text{CDCl}_3, 500 \text{ MHz}) \delta = 7.80 \text{ (d, } J = 8.5 \text{ Hz, 1H)}, 7.74 \text{ (d, } J = 7.0 \text{ Hz, 1H)}, 7.50 \text{ (s, 1H)}, 7.34-7.27 \text{ (m, 4H)}, 7.23 \text{ (s, 1H)}, 6.88-6.86 \text{ (m, 1H)}, 3.84 \text{ (s, 3H)}; \( ^{13}C \text{NMR} (\text{CDCl}_3, 125 \text{ MHz}) \delta = 159.9, 144.0, 140.6, 139.4, 135.6, 129.9, 124.5, 124.3, 123.5, 122.2, 119.6, 119.0, 113.7, 112.1, 55.2.

3-(benzo[b]thiophen-2-yl)phenol (2e): The product was purified by flash chromatography to give 64 mg (95%) as a white solid. \( ^1H \text{NMR} (\text{CDCl}_3, 500 \text{ MHz}) \delta = 7.82 \text{ (d, } J = 7.5 \text{ Hz, 1H}), 7.76 \text{ (d, } J = 7.5 \text{ Hz, 1H)}, 7.52 \text{ (s, 1H)}, 7.37-7.29 \text{ (m, 4H)}, 7.28 \text{ (s, 1H)}, 6.83-6.80 \text{ (m, 1H)}, 4.98 \text{ (s, 1H)}; \( ^{13}C \text{NMR} (\text{CDCl}_3, 125 \text{ MHz}) \delta = 155.9, 143.7, 140.5, 139.5, 135.9, 130.2, 124.5, 124.4, 123.6, 122.3, 119.8, 119.2, 115.2, 113.3.

4-(benzo[b]thiophen-2-yl)-N,N-dimethylaniline (2f): The product was purified by flash chromatography to give 70 mg (93%) as a white solid. \( ^1H \text{NMR} (\text{CDCl}_3, 500 \text{ MHz}) \delta = 7.77 \text{ (d, } J = 7.5 \text{ Hz, 1H}), 7.69 \text{ (d, } J = 8.0 \text{ Hz, 1H)}, 7.58 \text{ (d, } J = 9.0 \text{ Hz, 2H}), 7.35 \text{ (s, 1H)}, 7.30 \text{ (t, } J = 5.0 \text{ Hz, 1H)}, 7.23 \text{ (t, } J = 7.5 \text{ Hz, 1H)}, 6.74 \text{ (d, } J = 9.0 \text{ Hz, 2H}), 2.99 \text{ (s, 6H)}; \( ^{13}C \text{NMR} (\text{CDCl}_3, 125 \text{ MHz}) \delta = 150.4, 145.1, 141.1, 138.8, 127.4(2C), 124.3, 123.4, 122.9, 122.1, 116.6, 112.4, 40.4.

2-(4-chlorophenyl)benzo[b]thiophene (2g): The product was purified by flash chromatography to give 56 mg (77%) as a white solid. \( ^1H \text{NMR} (\text{CDCl}_3, 500 \text{ MHz}) \delta
= 7.82-7.81 (m, 1H), 7.76 (dd, $J = 1.5$, 7.0 Hz, 1H), 7.62 (dt, $J = 8.5$, 4.0 Hz, 2H), 7.50 (s, 1H), 7.40-7.35 (m, 2H), 7.34-7.30 (m, 2H). $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta =$ 142.8, 140.6, 139.5, 134.1, 132.8, 129.1, 127.6, 124.6, 124.5, 123.6, 122.3, 119.9.

2-(4-(trifluoromethyl)phenyl)benzo[b]thiophene(2h)$^5$: The product was purified by flash chromatography to give 80 mg (96%) as a white solid. $^1$H NMR (CDCl$_3$, 500 MHz) $\delta =$ 7.85 (d, $J = 8.0$ Hz, 1H), 7.81 (d, $J = 8.0$ Hz, 3H), 7.67 (d, $J = 8.0$ Hz, 2H), 7.63 (s, 1H), 7.40-7.34 (m, 2H); $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta =$ 142.3, 140.4, 139.8, 137.7, 130.0 (q, $J = 32.5$ Hz), 126.6, 125.9 (q, $J = 3.8$ Hz), 125.9, 125.0, 124.4 (q, $J =$ 270.3 Hz), 123.0, 122.3, 121.0.

4-(benzo[b]thiophen-2-yl)benzonitrile(2i)$^5$: The product was purified by flash chromatography to give 66 mg (94%) as a white solid. $^1$H NMR (CDCl$_3$, 500 MHz) $\delta =$ 7.85 (d, $J = 7.5$ Hz, 1H), 7.82-7.77 (m, 3H), 7.69 (d, $J = 8.5$ Hz, 2H), 7.65 (s, 1H), 7.40-7.35 (m, 2H); $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta =$ 141.6, 140.2, 139.9, 138.6, 132.7, 126.7, 125.3, 124.1, 124.1, 122.4, 121.7, 118.7, 111.3.

2-(naphthalen-2-yl)benzo[b]thiophene(2j)$^6$: The product was purified by flash chromatography to give 73 mg (94%) as a white solid. $^1$H NMR (CDCl$_3$, 500 MHz) $\delta =$ 8.14 (s, 1H), 7.89-7.83 (m, 5H), 7.80 (d, $J = 8.0$ Hz, 1H), 7.67 (s, 1H), 7.52-7.47 (m, 2H), 7.38-7.31 (m, 2H). $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta =$ 144.3, 140.8, 139.6, 133.5, 133.1, 131.6, 128.6, 128.2, 127.7, 126.7, 126.4, 125.3, 124.6, 124.4, 124.3, 123.6, 122.3, 119.9.
2-(naphthalen-1-yl)benzo[b]thiophene(2k): The product was purified by flash chromatography to give 71 mg (91%) as a white solid. \(^1\)H NMR (CDCl\(_3\), 500 MHz) \(\delta = 8.28\) (d, \(J = 9.0\) Hz, 1H), 7.90-7.86 (m, 3H), 7.82 (d, \(J = 7.5\) Hz, 1H), 7.64 (dd, \(J = 1.0, 7.0\) Hz, 1H), 7.51-7.48 (m, 3H), 7.43 (s, 1H), 7.41-7.33 (m, 2H). \(^{13}\)C NMR (CDCl\(_3\), 125 MHz) \(\delta = 142.1, 140.3, 140.2, 133.8, 132.4, 131.8, 128.9, 128.4, 128.3, 126.6, 126.1, 125.7, 125.2, 124.5, 124.2, 124.0, 123.6, 122.1.

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2-(thiophen-3-yl)benzo[b]thiophene(2l): The product was purified by flash chromatography to give 58 mg (90%) as a yellow solid. \(^1\)H NMR (CDCl\(_3\), 500 MHz) \(\delta = 7.77\) (d, \(J = 7\) Hz, 1H), 7.71 (d, \(J = 7\) Hz, 1H), 7.48 (s, 1H), 7.38-7.28 (m, 5H). \(^{13}\)C NMR (CDCl\(_3\), 125 MHz) \(\delta = 140.4, 139.0, 138.9, 135.7, 126.5, 126.1, 124.5, 124.2, 123.4, 122.2, 121.2, 119.3.

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4-(benzo[b]thiophen-2-yl)pyridine(2m): The product was purified by flash chromatography to give 60 mg (94%) as a white solid. \(^1\)H NMR (CDCl\(_3\), 500 MHz) \(\delta = 8.65\) (dd, \(J = 1.5, 4.5\) Hz, 2H), 7.87-7.81 (m, 2H), 7.74 (s, 1H), 7.58 (dd, \(J = 1.5, 4.5\) Hz, 2H), 7.41-7.36 (m, 2H). \(^{13}\)C NMR (CDCl\(_3\), 125 MHz) \(\delta = 150.3, 141.6, 140.8, 140.1, 139.9, 125.5, 124.9, 124.2, 122.4, 122.1, 120.5.

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2-(benzo[b]thiophen-2-yl)furan(2n): The product was purified by flash chromatography to give 37 mg (62%) as a yellow solid. \(^1\)H NMR (CDCl\(_3\), 500 MHz) \(\delta = 7.79\) (d, \(J = 8.0\) Hz, 1H), 7.74 (d, \(J = 7.5\) Hz, 1H), 7.47 (s, 2H), 7.35-7.28 (m, 2H), 6.63 (d, \(J = 3\) Hz, 1H), 6.48-6.47 (m, 1H). \(^{13}\)C NMR (CDCl\(_3\), 125 MHz) \(\delta = 149.3, 142.5, 140.2, 138.9, 133.3, 124.6, 124.4, 123.6, 122.2, 118.5, 111.9, 107.1.

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2-butylbenzo[b]thiophene (2o): The product was purified by flash chromatography to give 23 mg (41%) as oil. $^1$H NMR (CDCl$_3$, 500 MHz) $\delta$ = 7.75 (d, $J$ = 8.0 Hz, 1H), 7.64 (d, $J$ = 8.0 Hz, 1H), 7.30-7.27 (m, 1H), 7.24-7.21 (m, 1H), 6.98 (s, 1H), 2.89 (t, $J$ = 7.5 Hz, 2H), 1.76-1.70 (m, 2H), 1.44-1.40 (m, 2H), 0.95 (t, $J$ = 7.5 Hz, 3H). $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta$ = 146.8, 140.2, 139.2, 124.0, 123.3, 122.6, 122.1, 120.3, 33.2, 30.4, 22.2, 13.8.

2-(tert-buty)benzo[b]thiophene (2p): The product was purified by flash chromatography to give 17 mg (30%) as oil. $^1$H NMR (CDCl$_3$, 500 MHz) $\delta$ = 7.76 (d, $J$ = 8.0 Hz, 1H), 7.66 (d, $J$ = 8.0 Hz, 1H), 7.30 (t, $J$ = 4.0 Hz, 1H), 7.28-7.22 (m, 1H), 7.03 (s, 1H), 1.45 (s, 9H); $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta$ = 158.2, 140.0, 138.8, 123.9, 123.4, 122.8, 122.1, 117.6, 34.9, 32.2 (3C).

2-benzylbenzo[b]thiophene (2q): The product was purified by flash chromatography to give 14 mg (20%) as a white solid. $^1$H NMR (CDCl$_3$, 500 MHz) $\delta$ = 7.32 (d, $J$ = 8.0 Hz, 1H), 7.65 (d, $J$ = 7.5 Hz, 1H), 7.34-7.22 (m, 7H), 7.00 (s, 1H), 4.22 (s, 2H); $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta$ = 145.1, 140.0, 139.8, 139.5, 128.8 (2C), 128.6 (2C), 126.7, 124.1, 123.6, 122.9, 122.1, 121.6, 37.0.

5-methoxy-2-phenylbenzo[b]thiophene (2r): The product was purified by flash chromatography to give 37 mg (52%) as a white solid. $^1$H NMR (CDCl$_3$, 500 MHz) $\delta$ = 7.70-7.66 (m, 3H), 7.46 (s, 1H), 7.41 (t, $J$ = 7.5 Hz, 2H), 7.35-7.31 (m, 1H), 7.22 (s, 1H), 6.96 (dd, $J$ = 2.5, 8.5 Hz, 1H), 3.86 (s, 3H). $^{13}$C NMR (CDCl$_3$, 125 MHz) $\delta$ = 157.6, 145.5, 141.7, 134.4, 131.9, 128.9, 128.2, 126.4, 122.9, 119.3, 114.5, 105.7, 55.5.
6-methoxy-2-phenylbenzo[b]thiophene (2s): The product was purified by flash chromatography to give 45 mg (63%) as a white solid. \(^1\)H NMR (CDCl\(_3\), 500 MHz) \(\delta = 7.68-7.63\) (m, 3H), 7.45 (s, 1H), 7.40 (t, \(J = 7.8\) Hz, 2H), 7.32-7.29 (m, 2H), 6.97 (dd, \(J = 2.5, 9.0\) Hz, 1H), 3.87 (s, 3H). \(^{13}\)C NMR (CDCl\(_3\), 125 MHz) \(\delta = 157.5, 141.6, 141.0, 134.7, 134.5, 128.9, 127.8, 126.1, 124.2, 119.0, 114.5, 104.9, 55.6\).

5-chloro-2-phenylbenzo[b]thiophene (2t): The product was purified by flash chromatography to give 66 mg (90%) as a white solid. \(^1\)H NMR (CDCl\(_3\), 500 MHz) \(\delta = 7.74-7.69\) (m, 4H), 7.46-7.42 (m, 3H), 7.36 (t, \(J = 7.5\) Hz, 1H), 7.28-7.25 (m, 1H); \(^{13}\)C NMR (CDCl\(_3\), 125 MHz) \(\delta = 146.4, 141.8, 137.6, 133.8, 130.7, 129.0\) (2C), 128.7, 126.5 (2C), 124.7, 123.3, 123.0, 118.6.

5-chloro-2-phenylbenzo[b]thiophene (2u): The product was purified by flash chromatography to give 46 mg (63%) as a white solid. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta = 7.79\) (s, 1H), 7.69-7.66 (m, 3H), 7.49 (s, 1H), 7.44-7.41 (m, 2H), 7.37-7.34 (m, 1H), 7.31 (d, \(J = 8.5\) Hz, 1H); 13C NMR (125 MHz, CDCl\(_3\)) \(\delta = 144.9, 140.5, 139.1, 133.8, 130.3, 129.0, 128.5, 126.4, 125.3, 124.3, 121.8, 118.9; compound C \(^1\)H NMR (CDCl\(_3\), 500 MHz) \(\delta = 7.82\) (d, \(J = 8.0\) Hz, 1H), 7.77 (d, \(J = 7.5\) Hz, 1H), 7.72 (d, \(J = 8.5\) Hz, 2H), 7.54 (s, 0.8H ), 7.42 (t, \(J = 7.8\) Hz, 2H), 7.36-7.29 (m, 3H). \(^{13}\)C NMR (CDCl\(_3\), 125 MHz) \(\delta = 144.2, 140.6, 139.4, 134.2, 128.9, 128.2, 126.4, 124.5, 124.3, 123.5, 122.2, 119.4.

Reference:

5) Scanned $^1$H NMR and $^{13}$C NMR Spectra of All New Compounds
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