

**Iron(III) chloride-catalyzed mechanochemical cascade synthesis  
of highly-substituted pyrrolyl indoles**

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**Contents**

			Page No.
Experimental section	.....	.....	S2
<sup>1</sup> H & <sup>13</sup> C NMR Spectra	.....	.....	S4

## Experimental section:

**General information:** All commercially available chemicals were obtained from Aldrich and used without further purifications. The Retsch PM 100 planetary ball mill was used for all the reactions. A planetary Ball-milling apparatus Retsch PM100 was employed using four balls (stainless steel, size 10 mm). The reaction was performed in a 50 mL grinding jar. <sup>1</sup>H NMR (400 MHz), <sup>13</sup>C NMR (100 MHz), spectra were recorded on a Bruker DRX-400 Avance spectrometer with CDCl<sub>3</sub> as solvent. Elemental analyses were performed on a PE 2400 II CHN-analyzer (Perkin Elmer). All chemical shifts are given relative to residual signals of solvent. All yields refer to the isolated products.

**General Procedure for the Synthesis of Compounds 5.** A planetary ball milling apparatus Retsch PM100 was employed using four balls (stainless steel, size 10 mm). The reaction was performed in a 50 ml grinding jar. For each reaction a mixture of phenyl glyoxal **1** (1 mmol), aniline **2** (1 mmol), indole **3** (1 mmol) and FeCl<sub>3</sub> (20 mol%) was ball-milled for 30 min. Then dimethyl acetylenedicarboxylate (**4**, 1 mmol) was added, and the milling was continued for 3.5 h at 500 rpm at room temperature (a 30 min interval). After completion of the reaction (TLC monitoring), the reaction mixture was extracted with ethyl acetate (2 × 15 ml). The organic layer was washed with water (2 × 10 ml), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated under reduced pressure. The crude residue was subjected to column chromatography using light petroleum ethyl acetate mixtures as the eluent to obtain the analytically pure product.

**Dimethyl 5-(1H-indol-3-yl)-4-phenyl-1-(p-tolyl)-1H-pyrrole-2,3-dicarboxylate (5a):** White solid, mp. 185-187 °C, 398 mg (86% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.04 (brs, 1H), 7.26-7.25 (m, 3H), 7.22-7.10 (m, 7H), 7.08-7.02 (m, 2H), 6.90-6.87 (m, 1H), 6.74 (s, 1H), 8.85 (s, 3H), 3.73 (s, 3H), 2.29 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 167.4, 160.6, 138.0, 135.9, 135.3, 133.9, 131.9, 129.2, 128.9, 127.9, 127.2, 126.5, 126.1, 123.9, 122.9, 122.5, 122.0, 119.8, 111.0, 105.7, 52.4, 51.9, 21.1. Anal. Calcd. for C<sub>29</sub>H<sub>24</sub>N<sub>2</sub>O<sub>4</sub>: C, 74.98; H, 5.21; N, 6.03%; Found: C, 74.92; H, 5.16; N, 6.09%.

**Dimethyl 5-(2-methyl-1H-indol-3-yl)-4-phenyl-1-(p-tolyl)-1H-pyrrole-2,3-dicarboxylate (5b):** Gray solid, mp. 220-222 °C, 382 mg (80% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.75 (brs, 1H), 7.16-7.09 (m, 3H), 7.05-7.00 (m, 3H), 6.97-6.85 (m, 6H), 3.77 (s, 3H), 3.66 (s, 3H), 2.12 (s, 3H), 1.80 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 167.5, 160.9, 138.0, 135.9, 135.7, 135.1, 134.2, 131.7, 129.7, 129.1, 128.9, 128.1, 127.3, 126.6, 125.3, 123.5, 122.2, 121.3, 120.0, 119.1, 110.3, 103.1, 52.3, 51.9, 21.1, 12.2. Anal. Calcd. for C<sub>30</sub>H<sub>26</sub>N<sub>2</sub>O<sub>4</sub>: C, 75.30; H, 5.48; N, 5.85%; Found: C, 75.24; H, 5.40; N, 5.79%.

***Dimethyl 4-phenyl-5-(2-phenyl-1H-indol-3-yl)-1-(p-tolyl)-1H-pyrrole-2,3-dicarboxylate (5c):***

Brown gummy mass, 443 mg (82% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.06-8.00 (m, 2H), 7.61-7.59 (m, 2H), 7.39-7.36 (m, 4H), 7.16-7.07 (m, 4H), 6.74-6.68 (m, 4H), 6.57-6.55 (m, 2H), 5.45 (s, 1H), 3.82 (s, 3H), 3.59 (s, 3H), 2.09 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 165.4, 163.5, 152.1, 146.7, 139.9, 136.2, 136.0, 135.3, 131.3, 129.1, 128.7, 128.5, 128.3, 127.9, 127.1, 125.8, 123.2, 122.5, 122.2, 120.4, 111.0, 106.6, 104.3, 83.7, 53.0, 51.0, 20.8. Anal. Calcd. For C<sub>35</sub>H<sub>28</sub>N<sub>2</sub>O<sub>4</sub>: C, 77.76; H, 5.22; N, 5.18%; Found: C, 77.68; H, 5.17; N, 5.25%.

***Dimethyl 5-(5-methoxy-1H-indol-3-yl)-4-phenyl-1-(p-tolyl)-1H-pyrrole-2,3-dicarboxylate (5d):***

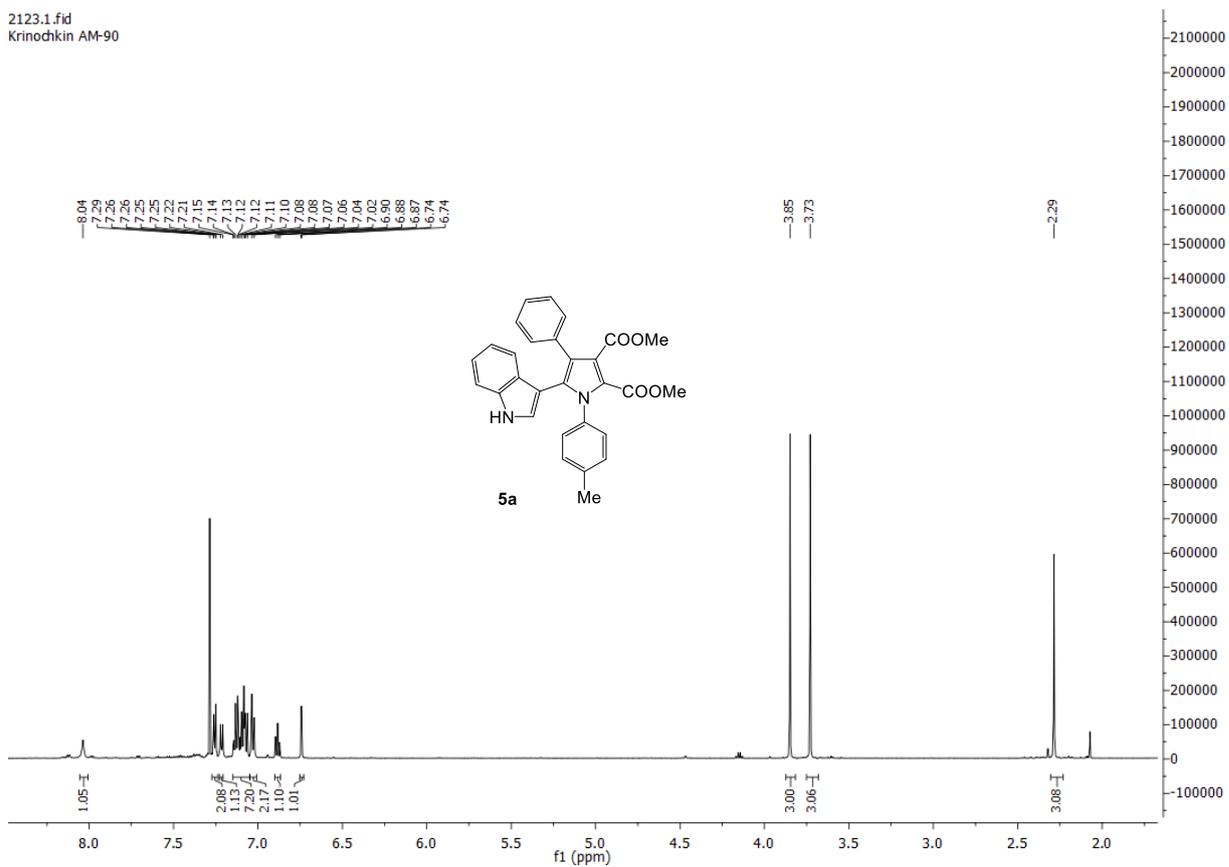
White solid, mp. 195-197 °C, 455 mg (92% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 7.94 (brs, 1H), 7.26-7.24 (m, 2H), 7.14-7.11 (m, 3H), 7.10-7.02 (m, 5H), 6.68-6.62 (m, 2H), 6.36 (s, 1H), 3.82 (s, 3H), 3.70 (s, 3H), 3.50 (s, 3H), 2.28 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 167.3, 160.5, 154.2, 138.2, 135.8, 133.9, 131.8, 130.0, 129.1, 129.0, 128.9, 127.9, 127.2, 126.5, 126.1, 123.1, 122.7, 122.5, 113.0, 111.3, 105.7, 100.7, 56.0, 53.0, 51.4, 21.9. Anal. Calcd. For C<sub>30</sub>H<sub>26</sub>N<sub>2</sub>O<sub>5</sub>: C, 72.86; H, 5.30; N, 5.66%; Found: C, 72.80; H, 5.21; N, 5.75%.

***Dimethyl 1-(4-chlorophenyl)-5-(1H-indol-3-yl)-4-phenyl-1H-pyrrole-2,3-dicarboxylate (5e):***

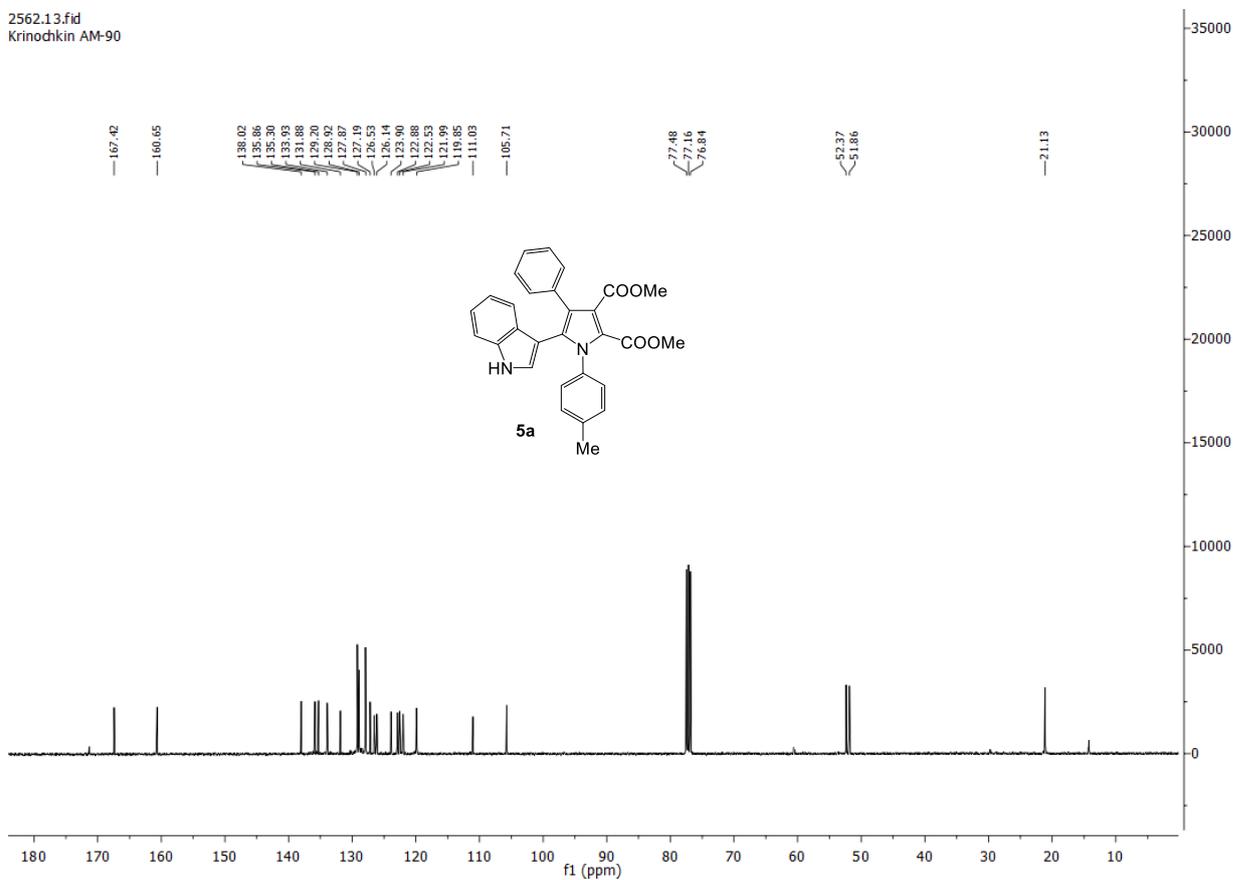
Pale yellow solid, mp. 212-214 °C, 368 mg (76% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.15 (brs, 1H), 7.26-7.07 (m, 12H), 6.94-6.90 (m, 1H), 6.76 (s, 1H), 3.86 (s, 3H), 3.75 (s, 3H); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 167.6, 160.8, 137.7, 135.8, 134.7, 134.1, 132.2, 130.1, 129.7, 129.1, 128.5, 127.6, 127.2, 126.4, 124.8, 123.9, 123.0(2C), 120.8, 120.3, 111.5, 106.4, 52.2, 51.8. Anal. Calcd. For C<sub>28</sub>H<sub>21</sub>ClN<sub>2</sub>O<sub>4</sub>: C, 69.35; H, 4.37; N, 5.78%; Found: C, 69.30; H, 4.45; N, 5.87%.

# $^1\text{H}$ and $^{13}\text{C}$ NMR Spectra

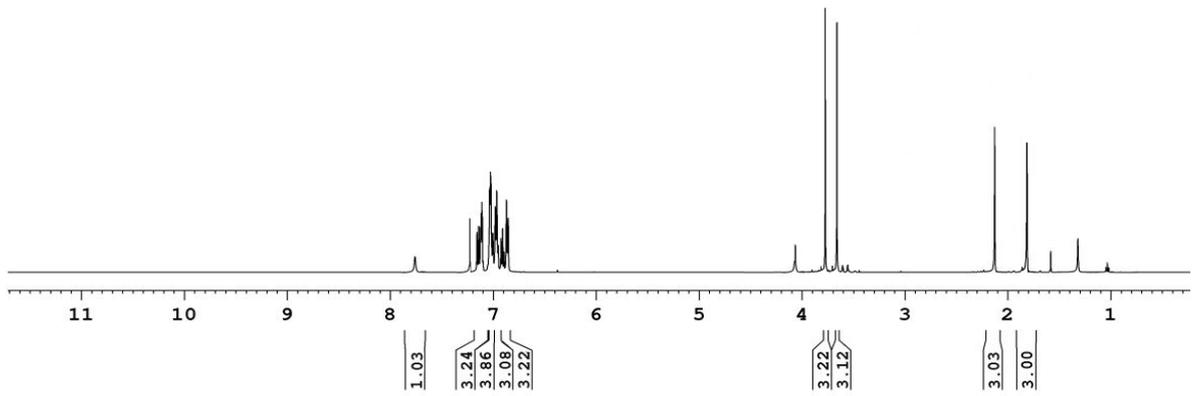
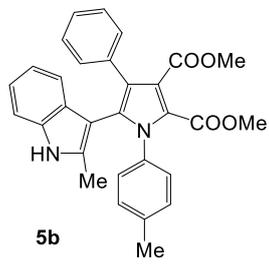
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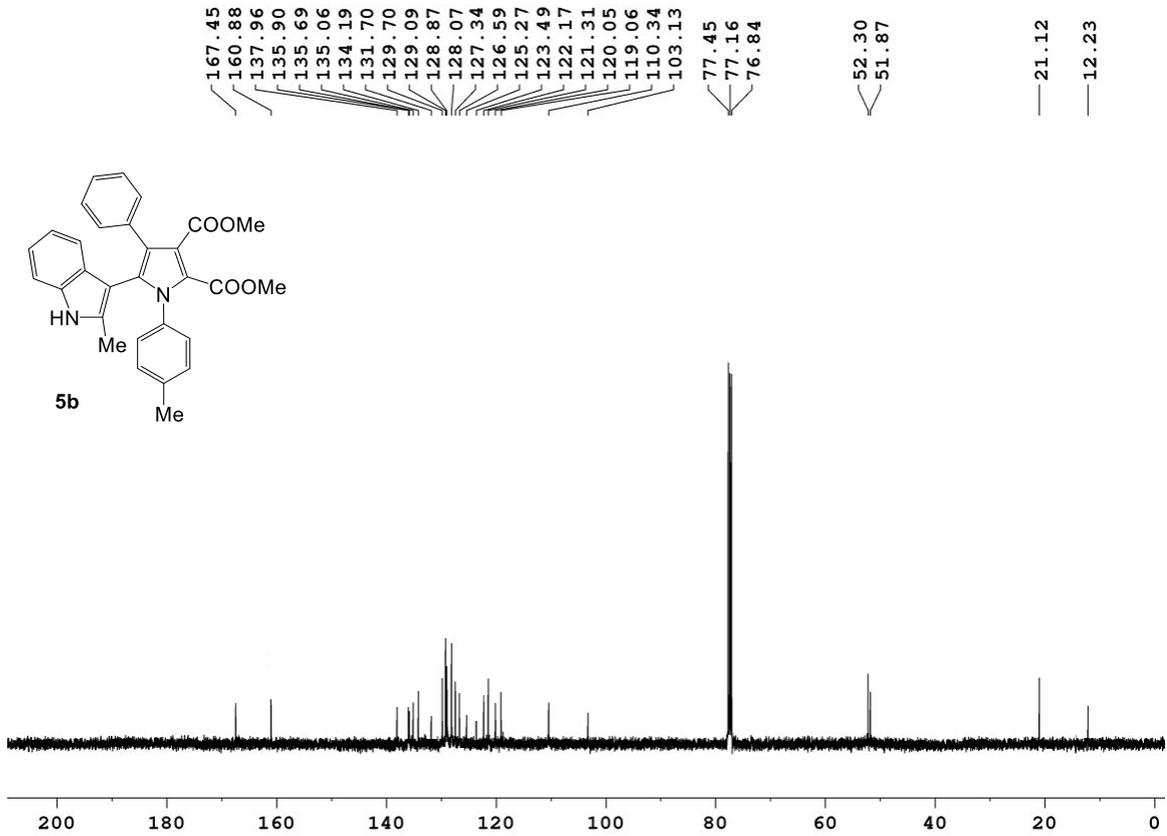
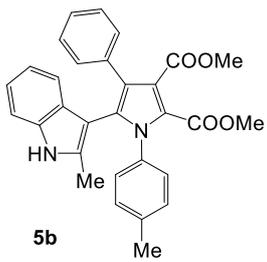


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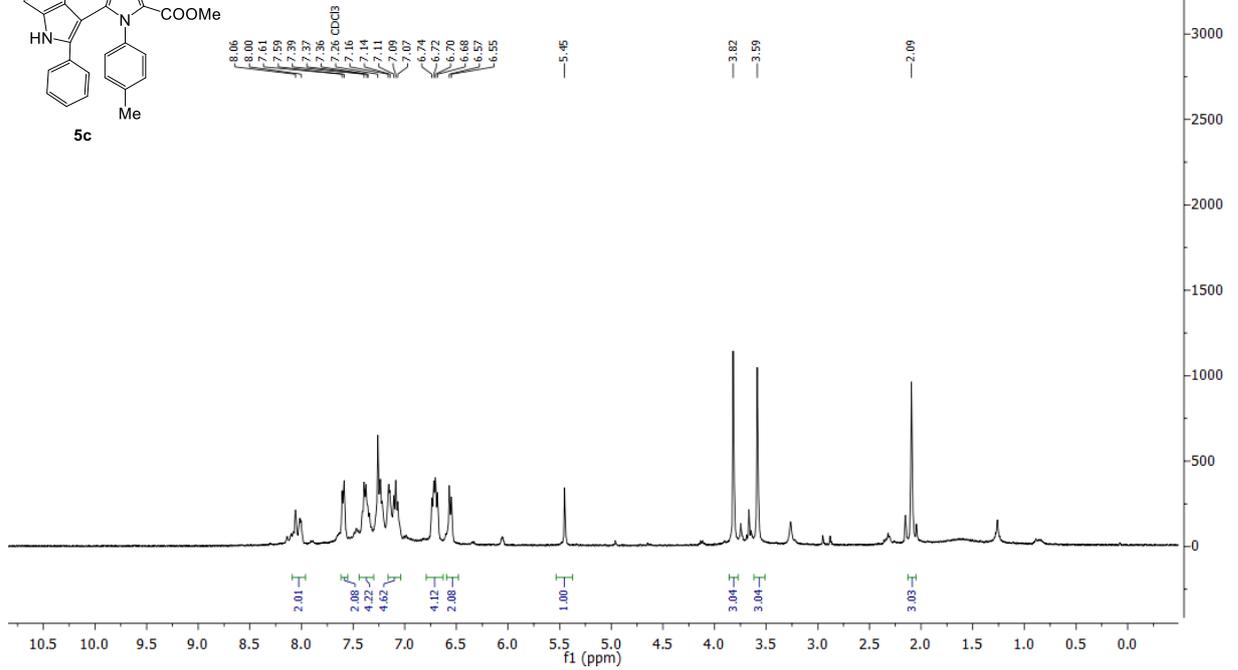
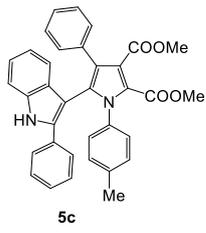
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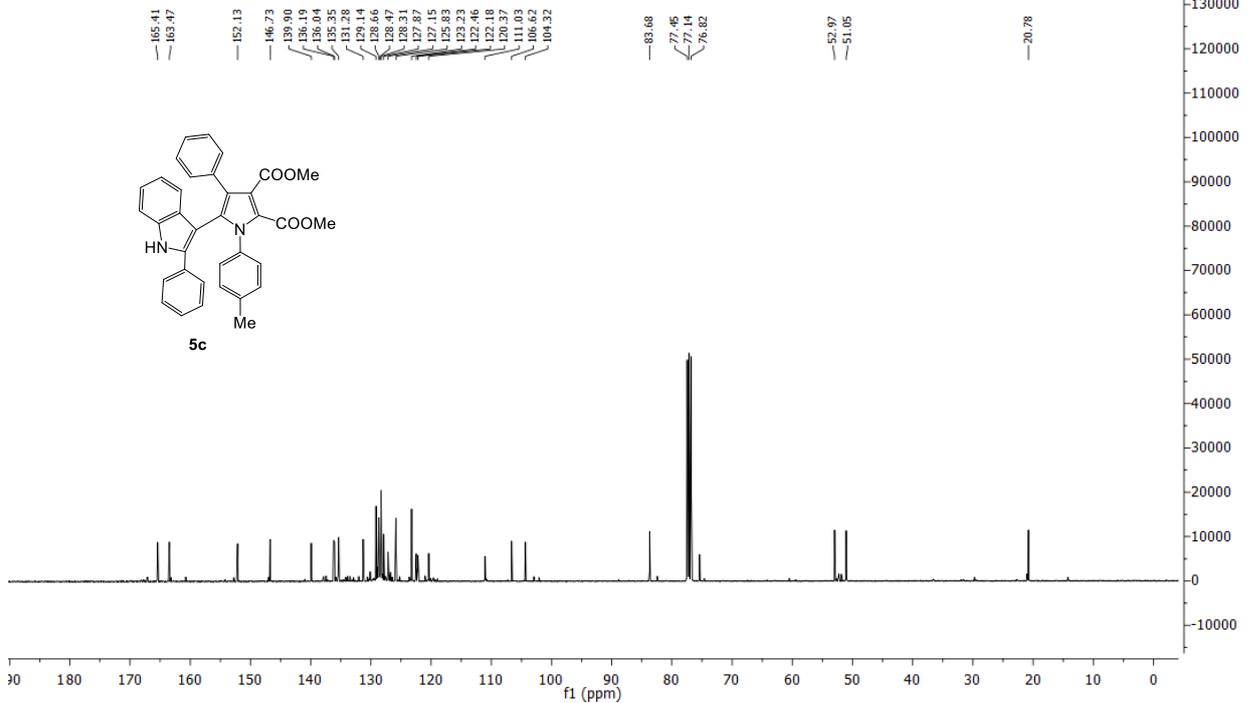
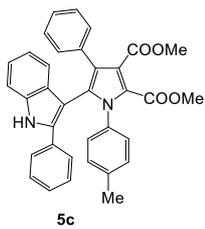
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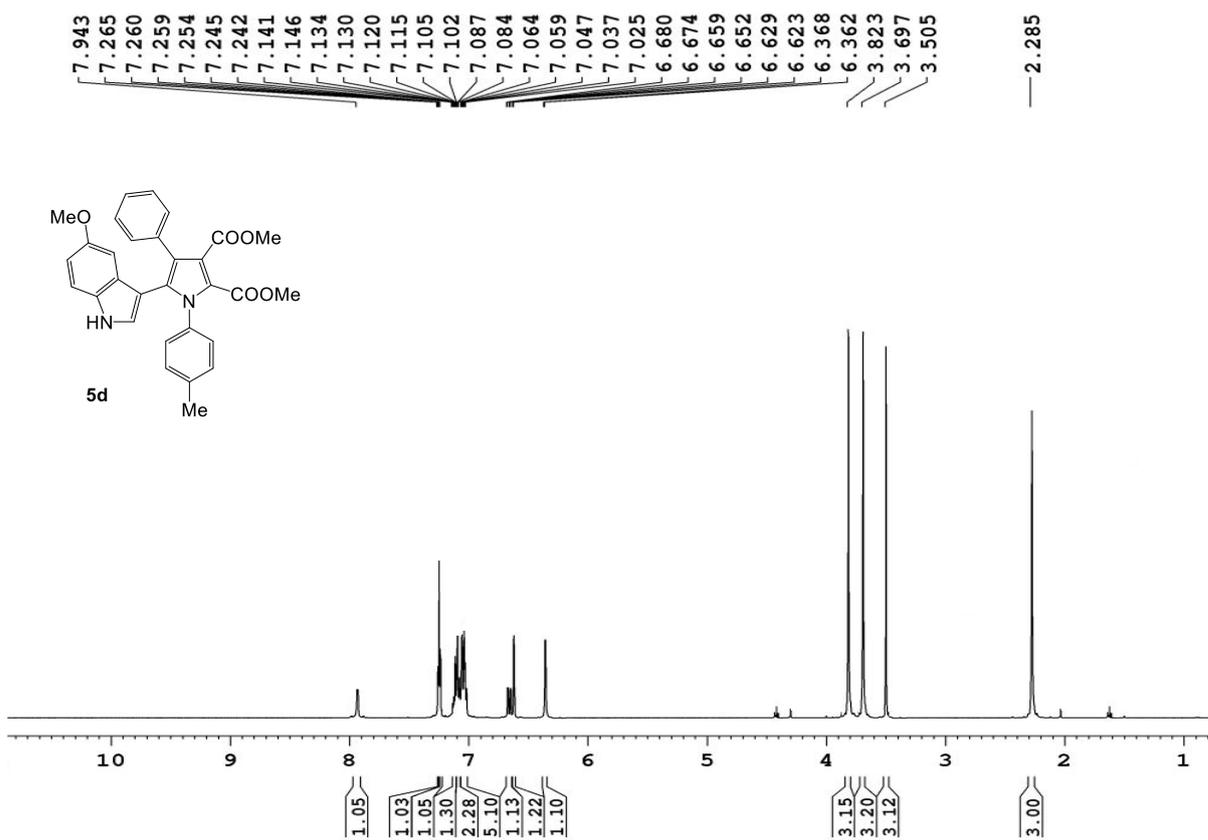
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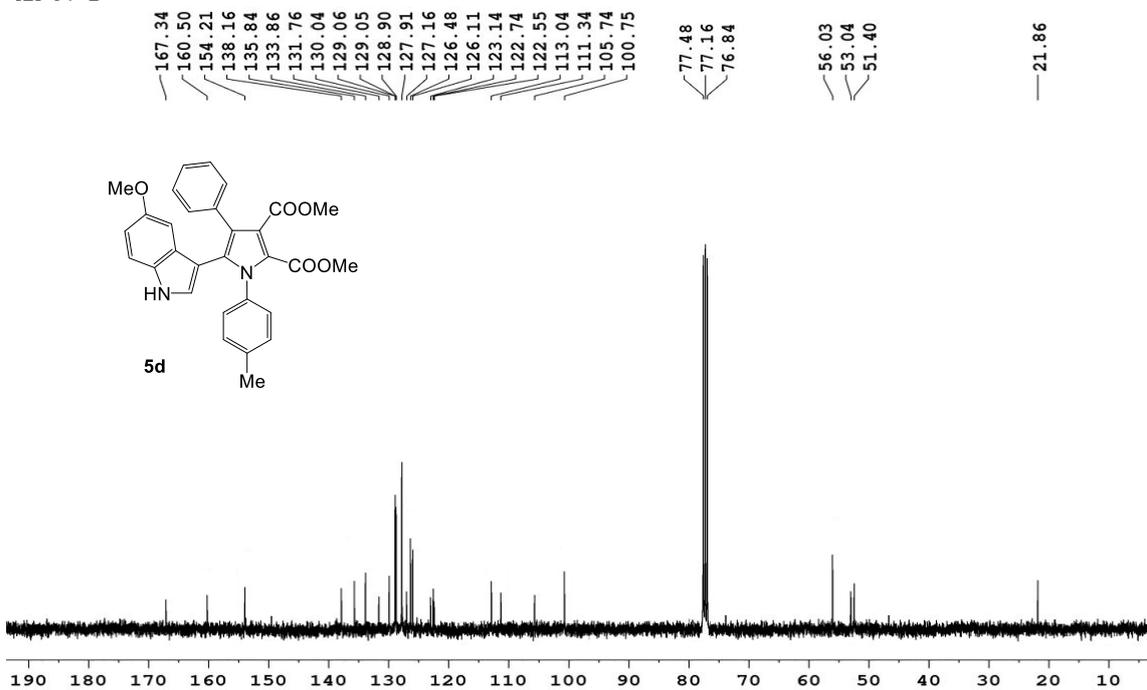
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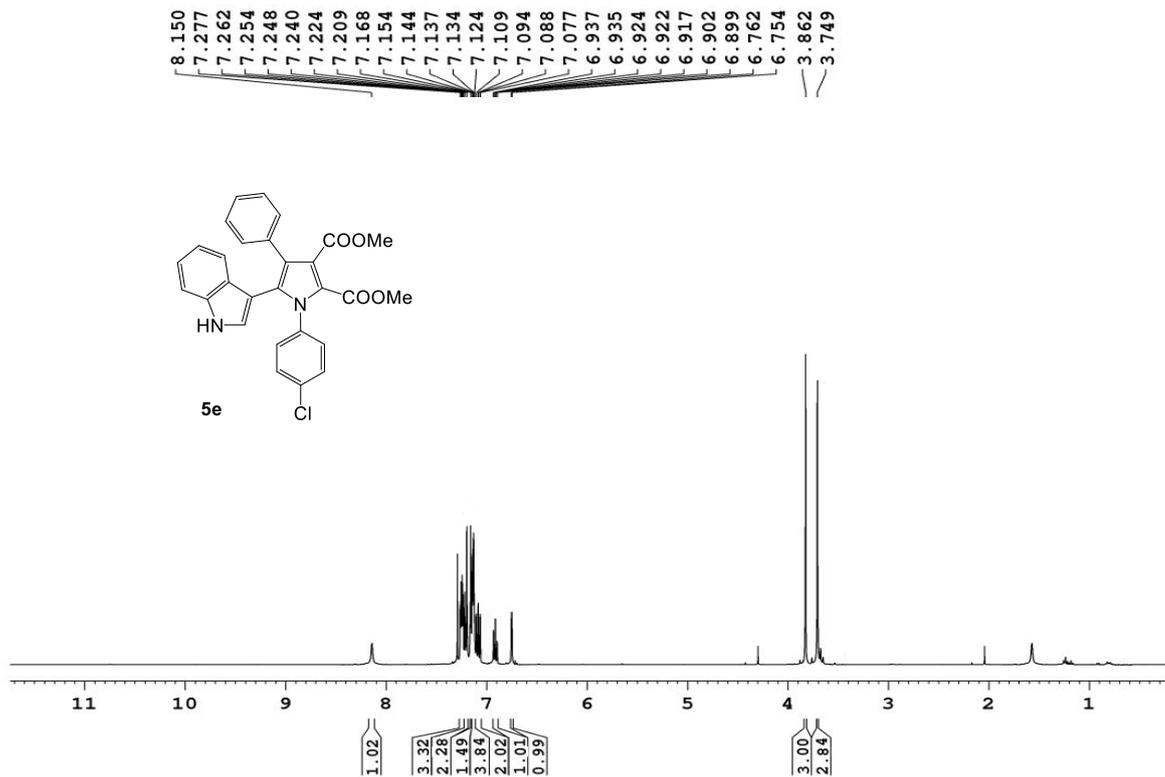
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