
Synthesis of Polycarbonyl Pyrroles via K₂S₂O₈-Mediated Oxidative Cyclization of Enamines

Peng Gao,^{*,†,‡} Juan Wang,[†] Zi-Jing Bai,[†] Li Shen,[†] Yun-Yun Yan,[†] De-Suo Yang,[†] Ming-Jin Fan,[†] Zheng-Hui Guan^{*,‡}.

[†]*Shaanxi Key Laboratory of Phytochemistry, College of Chemistry and Chemical Engineering, Baoji University of Arts and Sciences, Baoji, Shaanxi 721013, P. R. China*

[‡]*Key Laboratory of Synthetic and Natural Functional Molecule Chemistry of Ministry of Education, Department of Chemistry & Materials Science, Northwest University, Xi'an 710127, P. R. China*

gaopeng_hx@bjwlxy.edu.cn; guanzhh@nwu.edu.cn

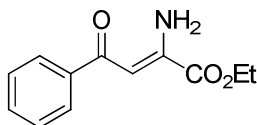
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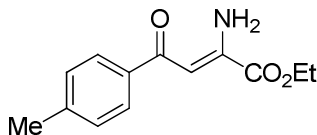
1. General Experimental Information and Materials

All solvents and reagents were obtained from commercial sources and used without further purification. ^1H NMR spectra obtained with tetramethylsilane (TMS, $\delta = 0$ ppm) as internal standard in CDCl_3 using a Agilent DD2 400-MR spectrometer (400 MHz). Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad), coupling constant (J) and integration. ^{13}C NMR spectra were recorded on Agilent DD2 400-MR spectrometer (100 MHz). The chemical shifts were determined in the δ -scale relative to CDCl_3 ($\delta = 77.0$ ppm). HR MS were recorded on an AB SCIEX TOFTM 4600 MS equipped with an electrospray ionization (ESI) probe operating in positive ion mode. Silica gel (200–300 mesh) was used for column chromatographic separations and purifications. Petroleum ether (PE) refers to the fraction boiling at 60–90 $^\circ\text{C}$.

Enamine compounds **1a–p** were prepared following our previous work¹ and **3a–l** were synthesized according to reported literatures.² **1a–o** are known compounds and the characterization data of **3a–l** were given as follows:



(Z)-ethyl 2-amino-4-oxo-4-phenylbut-2-enoate (3a). ^1H NMR (400 MHz, CDCl_3): δ 9.46 (br, 1H), 7.94–7.96 (m, 2H), 7.44–7.51 (m, 3H), 6.66 (s, 1H), 6.02 (br, 1H), 4.39 (q, $J = 7.1$ Hz, 2H), 1.41 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 192.0, 164.0, 147.6, 139.4, 132.0, 128.6, 127.6, 93.4, 62.9, 14.3. HRMS (ESI): m/z : calcd for $\text{C}_{12}\text{H}_{14}\text{NO}_3$ $[\text{M} + \text{H}]^+$ 220.0974, found: 220.0990.



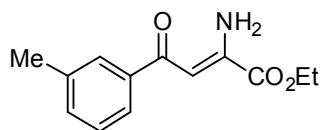
(Z)-ethyl 2-amino-4-oxo-4-(p-tolyl)but-2-enoate (3b). ^1H NMR (400 MHz, CDCl_3): δ 9.42 (br, 1H), 7.86 (d, $J = 8.2$ Hz, 2H), 7.24–7.26 (m, 2H), 6.64 (s, 1H), 5.95 (br, 1H), 4.39 (q, $J = 7.1$ Hz, 2H), 2.41 (s, 3H), 1.41 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz,

¹ Gao, P.; Liu, J.; Wei, Y. *Org. Lett.*, **2013**, *15*, 2872.

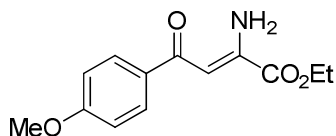
² Yu, W.; Du, Y.; Zhao, K. *Org. Lett.*, **2009**, *11*, 2417.

CDCl₃): δ 191.7, 164.1, 147.3, 142.6, 136.9, 129.3, 127.7, 93.4, 62.8, 21.7, 14.3.

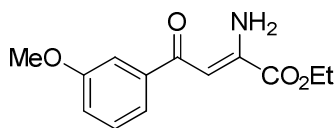
HRMS (ESI): m/z: calcd for C₁₃H₁₆NO₃ [M + H]⁺ 234.1130, found: 234.1127.



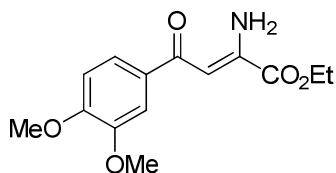
(Z)-ethyl 2-amino-4-oxo-4-(m-tolyl)but-2-enoate (3c). ¹H NMR (400 MHz, CDCl₃): δ 9.45 (br, 1H), 7.72-7.75 (m, 2H), 7.31-7.33 (m, 2H), 6.63 (s, 1H), 6.01 (br, 1H), 4.37 (q, J = 7.1 Hz, 2H), 2.41 (s, 1H), 1.39 (t, J = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 192.0, 163.9, 147.3, 139.3, 138.1, 132.6, 128.3, 128.0, 124.6, 93.4, 62.6, 21.4, 14.1. HRMS (ESI): m/z: calcd for C₁₃H₁₆NO₃ [M + H]⁺ 234.1130, found: 234.1133.



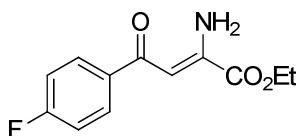
(Z)-ethyl 2-amino-4-(4-methoxyphenyl)-4-oxobut-2-enoate (3d). ¹H NMR (400 MHz, CDCl₃): δ 9.37 (br, 1H), 7.94 (d, J = 9.0 Hz, 2H), 6.94 (d, J = 9.0 Hz, 2H), 6.63 (s, 1H), 5.90 (br, 1H), 4.38 (q, J = 7.1 Hz, 2H), 3.87 (s, 3H), 1.40 (t, J = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 190.8, 164.2, 162.8, 147.1, 132.3, 129.7, 113.8, 93.1, 62.7, 55.6, 14.3. HRMS (ESI): m/z: calcd for C₁₃H₁₆NO₄ [M + H]⁺ 250.1079, found: 250.1072.



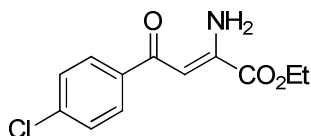
(Z)-ethyl 2-amino-4-(3-methoxyphenyl)-4-oxobut-2-enoate (3e) ¹H NMR (400 MHz, CDCl₃): δ 9.45 (br, 1H), 7.49-7.54 (m, 2H), 7.36 (t, J = 7.9 Hz, 1H), 7.05-7.07 (m, 1H), 6.63 (s, 1H), 6.02 (br, 1H), 4.39 (q, J = 7.1 Hz, 2H), 3.87 (s, 3H), 1.41 (t, J = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 191.7, 164.0, 160.0, 147.6, 140.9, 129.6, 120.1, 118.3, 112.2, 93.5, 62.9, 55.6, 14.3. HRMS (ESI): m/z: calcd for C₁₃H₁₆NO₄ [M + H]⁺ 250.1079, found: 250.1087.



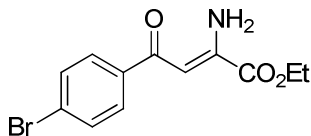
(Z)-ethyl 2-amino-4-(3,4-dimethoxyphenyl)-4-oxobut-2-enoate (3f). ^1H NMR (400 MHz, CDCl_3): δ 9.36 (br, 1H), 7.55-7.59 (m, 2H), 6.90 (d, $J = 8.3$ Hz, 1H), 6.64 (s, 1H), 5.94 (br, 1H), 4.39 (q, $J = 7.1$ Hz, 2H), 3.96 (s, 3H), 3.94 (s, 3H), 1.41 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 190.7, 164.1, 152.6, 149.2, 147.1, 132.5, 121.6, 110.3, 110.2, 93.2, 62.8, 56.2, 56.1, 14.3. HRMS (ESI): m/z : calcd for $\text{C}_{14}\text{H}_{18}\text{NO}_5$ $[\text{M} + \text{H}]^+$ 280.1185, found: 280.1185.



(Z)-ethyl 2-amino-4-(4-fluorophenyl)-4-oxobut-2-enoate (3g). ^1H NMR (400 MHz, CDCl_3): δ 9.43 (br, 1H), 7.95-7.99 (m, 2H), 7.12 (t, $J = 8.7$ Hz, 2H), 6.60 (s, 1H), 6.03 (br, 1H), 4.39 (q, $J = 7.1$ Hz, 2H), 1.41 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 190.4, 165.2 (d, $J_{\text{C-F}} = 252.6$ Hz), 163.9, 147.8, 135.7 (d, $J_{\text{C-F}} = 3.1$ Hz), 130.0 (d, $J_{\text{C-F}} = 9.1$ Hz), 115.6 (d, $J_{\text{C-F}} = 21.7$ Hz), 93.0, 62.9, 14.3. HRMS (ESI): m/z : calcd for $\text{C}_{12}\text{H}_{13}\text{FNO}_3$ $[\text{M} + \text{H}]^+$ 238.0879, found: 238.0874.

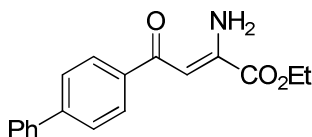


(Z)-ethyl 2-amino-4-(4-chlorophenyl)-4-oxobut-2-enoate (3h). ^1H NMR (400 MHz, CDCl_3): δ 9.48 (br, 1H), 7.74-8.01 (m, 2H), 7.31-7.51 (m, 2H), 6.56 (s, 1H), 6.10 (br, 1H), 4.36 (q, $J = 7.1$ Hz, 2H), 1.38 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 190.2, 163.6, 147.8, 138.0, 137.6, 128.8, 128.7, 92.7, 62.8, 14.1. HRMS (ESI): m/z : calcd for $\text{C}_{12}\text{H}_{13}\text{ClNO}_3$ $[\text{M} + \text{H}]^+$ 254.0584, found: 254.0582.

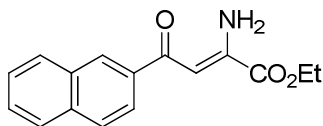


(Z)-ethyl 2-amino-4-(4-bromophenyl)-4-oxobut-2-enoate (3i). ^1H NMR (400 MHz,

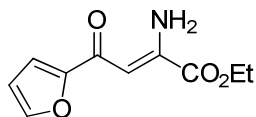
CDCl₃): δ 9.48 (br, 1H), 7.80-7.82 (m, 2H), 7.57-7.60 (m, 2H), 6.58 (s, 1H), 6.08 (br, 1H), 4.39 (q, J = 7.1 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 190.6, 163.8, 148.0, 138.2, 131.8, 129.2, 126.9, 92.9, 63.0, 14.3. HRMS (ESI): m/z : calcd for C₁₂H₁₃BrNO₃ [M + H]⁺ 298.0079, found: 298.0075.



(Z)-ethyl 4-([1,1'-biphenyl]-4-yl)-2-amino-4-oxobut-2-enoate (3j). ¹H NMR (400 MHz, CDCl₃): δ 9.49 (br, 1H), 8.02-8.05 (m, 2H), 7.63-7.07 (m, 4H), 7.45-7.49 (m, 2H), 7.37-7.41 (m, 1H), 6.70 (s, 1H), 6.03 (br, 1H), 4.41 (q, J = 7.2 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 191.4, 164.0, 147.6, 144.7, 140.3, 138.2, 129.0, 128.2, 128.1, 127.4, 127.3, 93.4, 62.9, 14.3. HRMS (ESI): m/z : calcd for C₁₈H₁₈NO₃ [M + H]⁺ 296.1287, found: 296.1274.



(Z)-ethyl 2-amino-4-(naphthalen-2-yl)-4-oxobut-2-enoate (3k). ¹H NMR (400 MHz, CDCl₃): δ 9.52 (br, 1H), 8.43-8.46 (m, 1H), 7.86-7.94 (m, 2H), 7.73-7.76 (m, 1H), 7.48-7.55 (m, 3H), 6.47 (s, 1H), 6.09 (br, 1H), 4.37 (q, J = 7.1 Hz, 2H), 1.37 (t, J = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 196.2, 164.0, 147.2, 139.2, 134.0, 131.1, 130.2, 128.5, 127.2, 126.3, 125.9, 124.8, 97.9, 62.9, 41.2, 14.2. HRMS (ESI): m/z : calcd for C₁₆H₁₆NO₃ [M + H]⁺ 270.1130, found: 270.1133.

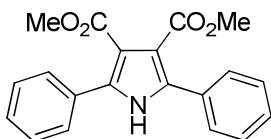


(Z)-ethyl 2-amino-4-(furan-2-yl)-4-oxobut-2-enoate (3l). ¹H NMR (400 MHz, CDCl₃): δ 9.21 (br, 1H), 7.55-7.55 (m, 1H), 7.13-7.14 (m, 1H), 6.50-6.52 (m, 2H), 5.96 (br, 1H), 4.37 (q, J = 7.1 Hz, 2H), 1.39 (t, J = 7.1 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 180.7, 163.8, 154.0, 147.5, 146.5, 114.8, 112.3, 93.3, 62.8, 14.2. HRMS (ESI): m/z : calcd for C₁₀H₁₂NO₄ [M + H]⁺ 210.0766, found: 210.0765.

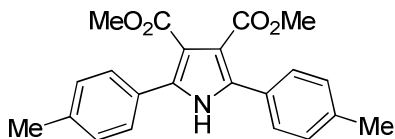
2. Experimental Procedures

A sealed tube was charged with enamine **1** or **3** (0.5 mmol), DMSO (5 mL), and then K₂S₂O₈ (0.6 mmol) was added. The reaction mixture was stirred at 100 °C for 5 h. Then the mixture was cooled to room temperature, and 20 mL water was added to the mixture, which was extracted with ethyl acetate (3 × 10 mL). The organic layer was combined and dried with anhydrous Na₂SO₄. After removal of the solvent under reduced pressure, the residue was separated by flash column chromatography to afford the pure product **2** or **4** (PE : EA = 10 : 1).

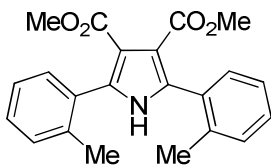
3. Characterization Data for the Products



Dimethyl 2,5-diphenyl-1H-pyrrole-3,4-dicarboxylate (2a). Light yellow solid (73 mg, 87% yield). mp 132-134 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.51 (br, 1H), 7.55-7.57 (m, 4H), 7.38-7.45 (m, 6H), 3.79 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 165.6, 134.4, 130.7, 128.6, 126.6, 128.0, 114.2, 51.9. HRMS (ESI): m/z calcd for C₂₀H₁₇NNaO₄ [M + Na]⁺ 358.1050, found: 358.1057.

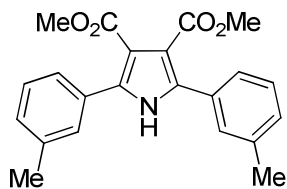


Dimethyl 2,5-di-p-tolyl-1H-pyrrole-3,4-dicarboxylate (2b). White solid (71 mg, 78% yield). mp 145-147 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.50 (br, 1H), 7.45 (d, *J* = 7.7 Hz, 4H), 7.22 (d, *J* = 7.8 Hz, 4H), 3.78 (s, 6H), 2.38 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 165.7, 138.6, 134.4, 129.3, 127.9, 113.7, 51.8, 21.3. HRMS (ESI): m/z calcd for C₂₂H₂₁NNaO₄ [M + Na]⁺ 386.1363, found: 386.1362.

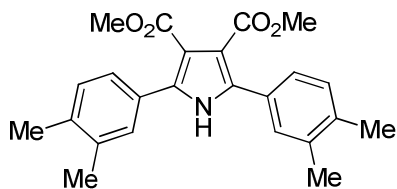


Dimethyl 2,5-di-o-tolyl-1H-pyrrole-3,4-dicarboxylate (2c). Light yellow solid (53 mg, 58% yield). mp 166-168 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.16 (br, 1H), 7.23-7.35

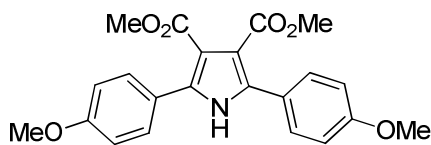
(m, 8H), 3.69 (s, 6H), 2.29 (s, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 165.3, 137.6, 134.5, 130.9, 130.7, 130.3, 129.3, 125.8, 114.6, 51.8, 20.2. HRMS (ESI): m/z calcd for $\text{C}_{22}\text{H}_{21}\text{NNaO}_4$ $[\text{M} + \text{Na}]^+$ 386.1363, found: 386.1370.



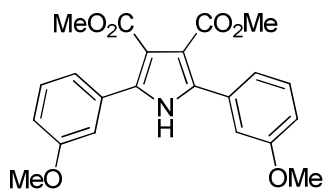
Dimethyl 2,5-di-*m*-tolyl-1H-pyrrole-3,4-dicarboxylate (2d). Light yellow solid (68 mg, 75% yield). mp 105-109 °C. ^1H NMR (400 MHz, CDCl_3): δ 8.48 (br, 1H), 7.28-7.37 (m, 6H), 7.19 (d, $J = 7.3$ Hz, 2H), 3.78 (s, 6H), 2.39 (s, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 165.9, 138.4, 134.6, 130.9, 129.5, 128.7, 128.6, 125.4, 114.2, 52.0, 21.6. HRMS (ESI): m/z calcd for $\text{C}_{22}\text{H}_{21}\text{NNaO}_4$ $[\text{M} + \text{Na}]^+$ 386.1363, found: 386.1371.



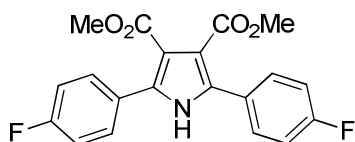
Dimethyl 2,5-bis(3,4-dimethylphenyl)-1H-pyrrole-3,4-dicarboxylate (2e). Light yellow solid (83 mg, 85% yield). mp 103-106 °C. ^1H NMR (400 MHz, CDCl_3): δ 8.34 (br, 1H), 7.30 (d, $J = 6.8$ Hz, 4H), 7.18 (d, $J = 8.3$ Hz, 2H), 3.79 (s, 6H), 2.30 (d, $J = 2.7$ Hz, 12H). ^{13}C NMR (100 MHz, CDCl_3): δ 165.9, 137.5, 137.0, 134.6, 130.0, 129.2, 128.5, 125.7, 113.9, 51.9, 20.0, 19.8. HRMS (ESI): m/z calcd for $\text{C}_{24}\text{H}_{25}\text{NNaO}_4$ $[\text{M} + \text{Na}]^+$ 414.1676, found: 414.1673.



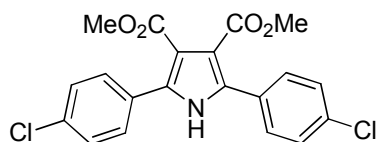
Dimethyl 2,5-bis(4-methoxyphenyl)-1H-pyrrole-3,4-dicarboxylate (2f). Light yellow solid (60 mg, 61% yield). mp 140-143 °C. ^1H NMR (400 MHz, CDCl_3): δ 8.50 (br, 1H), 7.49 (d, $J = 8.7$ Hz, 4H), 6.94 (d, $J = 8.7$ Hz, 4H), 3.83 (s, 6H), 3.77 (s, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 166.1, 160.1, 134.5, 129.7, 123.5, 114.2, 113.6, 55.6, 52.0. HRMS (ESI): m/z calcd for $\text{C}_{22}\text{H}_{21}\text{NNaO}_6$ $[\text{M} + \text{Na}]^+$ 418.1261, found: 418.1263.



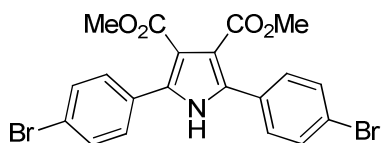
Dimethyl 2,5-bis(3-methoxyphenyl)-1H-pyrrole-3,4-dicarboxylate (2g). Light yellow solid (64 mg, 65% yield). mp 81-84 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.65 (br, 1H), 7.31 (t, *J* = 7.9 Hz, 2H), 7.09-7.13 (m, 4H), 6.89-6.92 (m, 2H), 3.82 (s, 6H), 3.78 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 165.8, 159.7, 134.2, 132.1, 129.8, 120.4, 114.5, 114.4, 113.8, 55.5, 52.1. HRMS (ESI): *m/z* calcd for C₂₂H₂₁NNaO₆ [M + Na]⁺ 418.1261, found: 418.1268.



Dimethyl 2,5-bis(4-fluorophenyl)-1H-pyrrole-3,4-dicarboxylate (2h). White solid (80 mg, 86% yield). mp 168-171 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.70 (br, 1H), 7.52-7.55 (m, 4H), 7.11 (t, *J* = 8.6 Hz, 4H), 3.77 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 165.6, 163.1 (d, *J*_{C-F} = 249 Hz), 133.8, 130.3 (d, *J*_{C-F} = 8.4 Hz), 126.9 (d, *J*_{C-F} = 3.5 Hz), 115.8 (d, *J*_{C-F} = 21.8 Hz), 52.1. HRMS (ESI): *m/z* calcd for C₂₀H₁₅F₂NNaO₄ [M + Na]⁺ 394.0861, found: 394.0859.

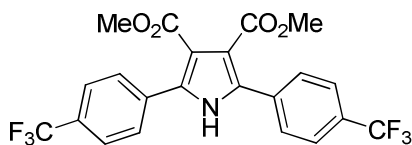


Dimethyl 2,5-bis(4-chlorophenyl)-1H-pyrrole-3,4-dicarboxylate (2i). Light yellow solid (85 mg, 84% yield). mp 188-192 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.73 (s, 1H), 7.46 (d, *J* = 8.4 Hz, 4H), 7.35 (d, *J* = 8.4 Hz, 4H), 3.76 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 165.3, 134.6, 133.3, 129.2, 128.8, 128.6, 114.4, 51.8. HRMS (ESI): *m/z* calcd for C₂₀H₁₅Cl₂NNaO₄ [M + Na]⁺ 426.0270, found: 426.0277.



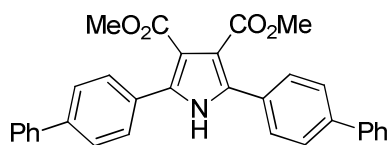
Dimethyl 2,5-bis(4-bromophenyl)-1H-pyrrole-3,4-dicarboxylate (2j). White solid

(109 mg, 89% yield). mp 175-177 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.49 (s, 1H), 7.56 (d, *J* = 8.5 Hz, 4H), 7.43 (d, *J* = 8.5 Hz, 4H), 3.79 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 165.4, 133.7, 132.0, 129.8, 129.6, 123.3, 114.9, 52.2. HRMS (ESI): *m/z* calcd for C₂₀H₁₅Br₂NNaO₄ [M + Na]⁺ 515.9245, found: 515.9241.



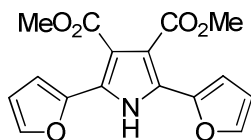
Dimethyl 2,5-bis(4-(trifluoromethyl)phenyl)-1H-pyrrole-3,4-dicarboxylate (2k).

White solid (98 mg, 83% yield). mp 181-183 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.77 (s, 1H), 7.67 (s, 8H), 3.79 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 165.3, 134.0, 133.5, 131.1, 130.7, 128.5, 125.8 (q, *J*_{C-F} = 3.8 Hz), 115.7, 52.3. HRMS (ESI): *m/z* calcd for C₂₂H₁₅F₆NNaO₄ [M + Na]⁺ 494.0797, found: 494.0791.



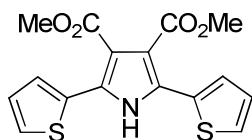
Dimethyl 2,5-di([1,1'-biphenyl]-4-yl)-1H-pyrrole-3,4-dicarboxylate (2l).

White solid (89 mg, 73% yield). mp 212-215 °C. ¹H NMR (400 MHz, CDCl₃): δ 8.82 (br, 1H), 7.65 (s, 8H), 7.61-7.63 (m, 4H), 7.46 (t, *J* = 7.5 Hz, 4H), 7.35-7.39 (m, 2H), 3.82 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 165.9, 141.5, 140.4, 134.4, 129.8, 129.0, 128.6, 127.8, 127.4, 127.2, 114.5, 52.1. HRMS (ESI): *m/z*: calcd for C₃₂H₂₅NNaO₄ [M + Na]⁺ 510.1676, found: 510.1684.

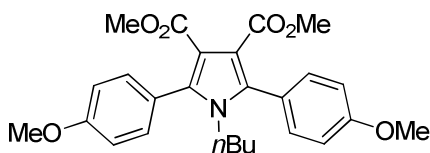


Dimethyl 2,5-di(furan-2-yl)-1H-pyrrole-3,4-dicarboxylate (2m).

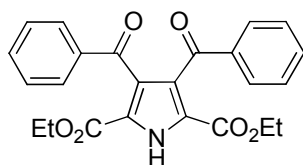
Brown liquid (44 mg, 56% yield). ¹H NMR (400 MHz, CDCl₃): δ 9.26 (s, 1H), 7.45-7.46 (m, 2H), 7.11-7.12 (m, 2H), 6.50-6.51 (m, 4H), 3.87 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 165.1, 144.6, 142.2, 125.6, 112.5, 112.4, 110.2, 52.1. HRMS (ESI): *m/z* calcd for C₁₆H₁₃NNaO₆ [M + Na]⁺ 338.0635, found: 338.0640.



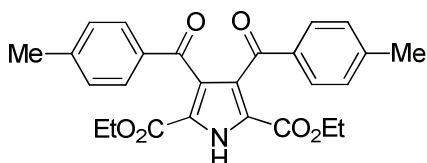
Dimethyl 2,5-di(thiophen-2-yl)-1H-pyrrole-3,4-dicarboxylate (2n). Light yellow solid (50 mg, 58% yield). mp 181-183 °C. ^1H NMR (400 MHz, CDCl_3): δ 8.69 (s, 1H), 7.41 (dd, J = 3.6, 1.2 Hz, 2H), 7.37 (dd, J = 5.1, 1.2 Hz, 2H), 7.08 (dd, J = 5.1, 3.7 Hz, 2H), 3.82 (s, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 165.1, 131.4, 128.5, 127.7, 127.6, 126.8, 114.7, 52.1. HRMS (ESI): m/z calcd for $\text{C}_{16}\text{H}_{13}\text{NNaO}_4\text{S}_2$ $[\text{M} + \text{Na}]^+$ 370.0178, found: 370.0176.



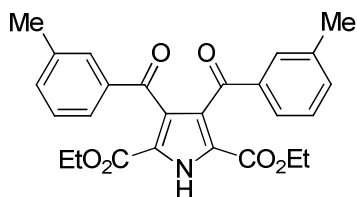
Dimethyl 1-butyl-2,5-bis(4-methoxyphenyl)-1H-pyrrole-3,4-dicarboxylate (2o). Light yellow solid (49 mg, 43% yield). mp 106-108 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.31-7.34 (m, 4H), 6.94-6.98 (m, 4H), 3.86 (s, 6H), 3.66 (m, 8H), 1.12-1.26 (m, 2H), 0.83-0.88 (m, 2H), 0.54 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 165.8, 159.9, 136.4, 131.9, 123.3, 114.3, 113.8, 55.4, 51.7, 44.7, 32.6, 19.5, 13.4. HRMS (ESI): m/z : calcd for $\text{C}_{26}\text{H}_{29}\text{NNaO}_6$ $[\text{M} + \text{Na}]^+$ 474.1887, found: 474.1886.



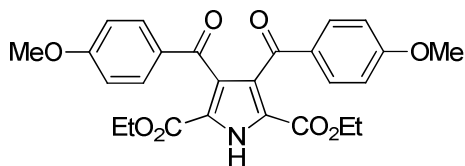
Diethyl 3,4-dibenzoyl-1H-pyrrole-2,5-dicarboxylate (4a). Light yellow solid (85 mg, 81% yield). mp 168-170 °C. ^1H NMR (400 MHz, CDCl_3): δ 10.10 (s, 1H), 7.80-7.83 (m, 4H), 7.51-7.55 (m, 2H), 7.37-7.41 (m, 4H), 4.06 (q, J = 7.2 Hz, 4H), 0.87 (t, J = 7.2 Hz, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 191.3, 159.4, 138.2, 133.4, 129.6, 129.3, 128.5, 123.8, 62.0, 13.5. HRMS (ESI): m/z calcd for $\text{C}_{24}\text{H}_{21}\text{NNaO}_6$ $[\text{M} + \text{Na}]^+$ 442.1261, found: 442.1267.



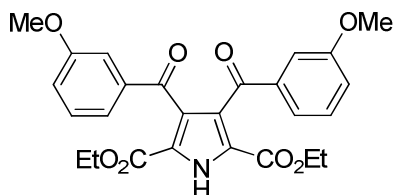
Diethyl 3,4-bis(4-methylbenzoyl)-1H-pyrrole-2,5-dicarboxylate (4b). Light yellow solid (89 mg, 80% yield). mp 171-173 °C. ¹H NMR (400 MHz, CDCl₃): δ 10.07 (s, 1H), 7.70 (d, *J* = 8.2 Hz, 4H), 7.18 (d, *J* = 8.0 Hz, 4H), 4.08 (q, *J* = 7.2 Hz, 4H), 2.38 (s, 6H), 0.91 (t, *J* = 7.1 Hz, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 191.0, 159.4, 144.3, 135.7, 129.8, 129.3, 129.1, 123.6, 61.9, 21.9, 13.6. HRMS (ESI): *m/z* calcd for C₂₆H₂₅NNaO₆ [*M* + Na]⁺ 470.1574, found: 470.1566.



Diethyl 3,4-bis(3-methylbenzoyl)-1H-pyrrole-2,5-dicarboxylate (4c). Light yellow solid (64 mg, 57% yield). mp 167-169 °C. ¹H NMR (400 MHz, CDCl₃): δ 7.56-7.60 (m, 4H), 7.23-7.33 (m, 4H), 4.07 (q, *J* = 7.2 Hz, 4H), 2.32 (s, 6H), 0.88 (t, *J* = 7.1 Hz, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 191.3, 159.4, 138.0, 137.9, 134.0, 129.8, 129.2, 128.1, 126.9, 123.7, 61.7, 21.2, 13.4. HRMS (ESI): *m/z* calcd for C₂₆H₂₅NNaO₆ [*M* + Na]⁺ 470.1574, found: 470.1576.

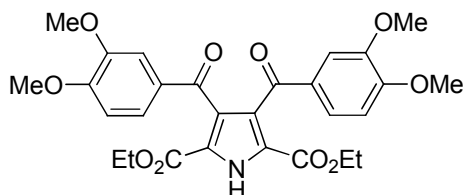


Diethyl 3,4-bis(4-methoxybenzoyl)-1H-pyrrole-2,5-dicarboxylate (4d). Light yellow solid (85 mg, 71% yield). mp 170-172 °C. ¹H NMR (400 MHz, CDCl₃): δ 10.00 (s, 1H), 7.77 (d, *J* = 8.9 Hz, 4H), 6.86 (d, *J* = 8.9 Hz, 4H), 4.11 (q, *J* = 7.1 Hz, 4H), 3.84 (s, 6H), 0.96 (t, *J* = 7.1 Hz, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 189.9, 163.9, 159.5, 132.1, 131.3, 129.3, 123.4, 113.7, 61.9, 55.6, 13.7. HRMS (ESI): *m/z* calcd for C₂₆H₂₅NNaO₈ [*M* + Na]⁺ 502.1472, found: 502.1476.

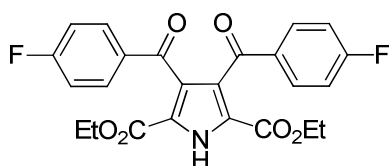


Diethyl 3,4-bis(3-methoxybenzoyl)-1H-pyrrole-2,5-dicarboxylate (4e). Light yellow solid (91 mg, 76% yield). mp 106-108 °C. ¹H NMR (400 MHz, CDCl₃): δ 10.12 (s,

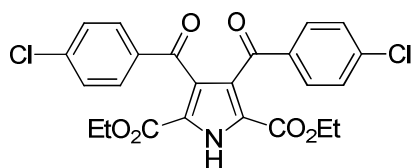
1H), 7.24-7.38 (m, 7H), 7.06-7.09 (m, 2H), 4.10 (q, $J = 7.2$ Hz, 4H), 3.80 (s, 6H), 0.94 (t, $J = 7.1$ Hz, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 190.8, 159.6, 159.2, 139.3, 129.2, 129.0, 123.6, 122.8, 120.1, 112.8, 61.8, 55.4, 13.5. HRMS (ESI): m/z calcd for $\text{C}_{26}\text{H}_{25}\text{NNaO}_8$ $[\text{M} + \text{Na}]^+$ 502.1472, found: 502.1479.



Diethyl 3,4-bis(3,4-dimethoxybenzoyl)-1H-pyrrole-2,5-dicarboxylate (4f). Light yellow solid (109 mg, 81% yield). mp 108-110 °C. ^1H NMR (400 MHz, CDCl_3): δ 10.09 (s, 1H), 7.42 (d, $J = 2.0$ Hz, 2H), 7.33 (dd, $J = 8.4, 2.0$ Hz, 2H), 6.80 (d, $J = 8.4$ Hz, 2H), 4.14 (q, $J = 7.1$ Hz, 4H), 3.91 (s, 6H), 3.86 (s, 6H), 1.01 (t, $J = 7.1$ Hz, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 189.7, 159.3, 153.6, 148.9, 131.1, 128.9, 125.7, 123.3, 110.5, 109.7, 61.7, 56.0, 55.9, 13.6. HRMS (ESI): m/z calcd for $\text{C}_{28}\text{H}_{29}\text{NNaO}_{10}$ $[\text{M} + \text{Na}]^+$ 562.1684, found: 562.1681.

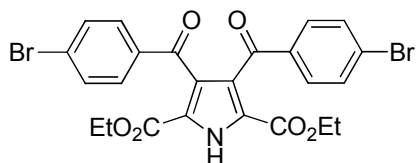


Diethyl 3,4-bis(4-fluorobenzoyl)-1H-pyrrole-2,5-dicarboxylate (4g). Light yellow solid (72 mg, 63% yield). mp 166-167 °C. ^1H NMR (400 MHz, CDCl_3): δ 10.19 (s, 1H), 7.82-7.86 (m, 4H), 7.08 (t, $J = 8.6$ Hz, 4H), 4.11 (q, $J = 7.1$ Hz, 4H), 0.94 (t, $J = 7.1$ Hz, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 189.8, 166.1 ($J_{\text{C-F}} = 260.0$ Hz), 159.2, 134.6 (d, $J_{\text{C-F}} = 2.9$ Hz), 132.3 (d, $J_{\text{C-F}} = 9.5$ Hz), 128.9, 123.8, 115.7 (d, $J = 22.1$ Hz), 62.1, 13.6. HRMS (ESI): m/z calcd for $\text{C}_{24}\text{H}_{19}\text{F}_2\text{NNaO}_6$ $[\text{M} + \text{Na}]^+$ 478.1073, found: 478.1074.

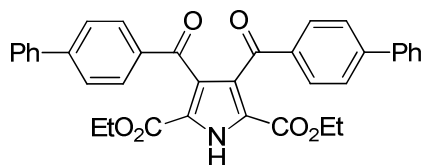


Diethyl 3,4-bis(4-chlorobenzoyl)-1H-pyrrole-2,5-dicarboxylate (4h). Light yellow solid (82 mg, 67% yield). mp 146-149 °C. ^1H NMR (400 MHz, CDCl_3): δ 10.09 (s,

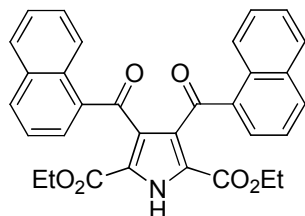
1H), 7.75 (d, $J = 8.5$ Hz, 4H), 7.39 (d, $J = 8.5$ Hz, 4H), 4.11 (q, $J = 7.1$ Hz, 4H), 0.95 (t, $J = 7.1$ Hz, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 190.1, 159.1, 140.1, 136.5, 131.0, 128.9, 123.8, 62.2, 13.7. HRMS (ESI): m/z : calcd for $\text{C}_{24}\text{H}_{19}\text{Cl}_2\text{NNaO}_6$ $[\text{M} + \text{Na}]^+$ 510.0482, found: 510.0482.



Diethyl 3,4-bis(4-bromobenzoyl)-1H-pyrrole-2,5-dicarboxylate (4i). White solid (105 mg, 73% yield). mp 166-167 °C. ^1H NMR (400 MHz, CDCl_3): δ 10.15 (s, 1H), 7.67 (d, $J = 8.5$ Hz, 4H), 7.56 (d, $J = 8.5$ Hz, 4H), 4.11 (q, $J = 7.1$ Hz, 4H), 0.95 (t, $J = 7.1$ Hz, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 190.3, 159.1, 136.9, 131.9, 131.0, 128.8, 128.7, 123.9, 62.2, 13.7. HRMS (ESI): m/z calcd for $\text{C}_{24}\text{H}_{20}\text{Br}_2\text{NO}_6$ $[\text{M} + \text{H}]^+$ 575.9652, found: 575.9661.

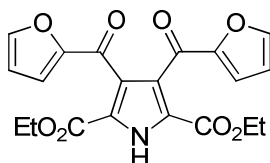


Diethyl 3,4-di([1,1'-biphenyl]-4-carbonyl)-1H-pyrrole-2,5-dicarboxylate (4j). White solid (117 mg, 82% yield). mp 213-215 °C. ^1H NMR (400 MHz, CDCl_3): δ 10.14 (s, 1H), 7.89-7.92 (m, 4H), 7.59-7.64 (m, 8H), 7.37-7.48 (m, 6H), 4.11 (q, $J = 7.2$ Hz, 4H), 0.93 (t, $J = 7.1$ Hz, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 190.9, 159.4, 146.1, 140.1, 137.0, 130.3, 129.4, 129.1, 128.4, 127.4, 127.1, 123.8, 62.0, 13.6. HRMS (ESI): m/z calcd for $\text{C}_{36}\text{H}_{29}\text{NNaO}_6$ $[\text{M} + \text{Na}]^+$ 594.1887, found: 594.1821.

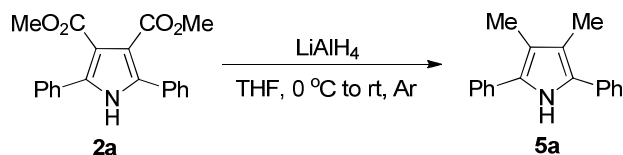


Diethyl 3,4-di(2-naphthoyl)-1H-pyrrole-2,5-dicarboxylate (4k). Light yellow solid (74 mg, 57% yield). mp 201-202 °C. ^1H NMR (400 MHz, CDCl_3): δ 10.13 (s, 1H), 8.66-8.69 (m, 2H), 7.93 (d, $J = 8.2$ Hz, 2H), 7.85 (dd, $J = 7.2, 1.2$ Hz, 2H), 7.78-7.80

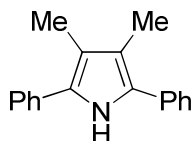
(m, 2H), 7.40-7.48 (m, 6H), 3.90 (q, $J = 7.2$ Hz, 4H), 0.61 (t, $J = 7.1$ Hz, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 192.5, 159.4, 135.5, 133.7, 133.5, 131.8, 131.4, 130.6, 128.1, 128.0, 126.3, 125.8, 124.1, 123.6, 61.7, 13.2. HRMS (ESI): m/z calcd for $\text{C}_{32}\text{H}_{25}\text{NNaO}_6$ $[\text{M} + \text{Na}]^+$ 542.1574, found: 542.1564.



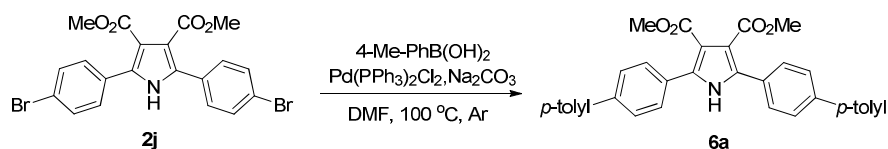
Diethyl 3,4-di(furan-2-carbonyl)-1H-pyrrole-2,5-dicarboxylate (4l). (81 mg, 81% yield). ^1H NMR (400 MHz, CDCl_3): δ 10.08 (s, 1H), 7.54 (d, $J = 1.0$ Hz, 2H), 7.11 (d, $J = 3.6$ Hz, 2H), 6.52 (dd, $J = 3.6, 1.6$ Hz, 2H), 4.20 (q, $J = 7.1$ Hz, 4H), 1.09 (t, $J = 7.1$ Hz, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 177.7, 159.4, 153.5, 147.0, 127.6, 124.0, 119.5, 112.8, 62.1, 13.9. HRMS (ESI): m/z calcd for $\text{C}_{20}\text{H}_{17}\text{NNaO}_8$ $[\text{M} + \text{Na}]^+$ 422.0846, found: 422.0849.



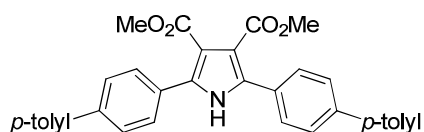
To a solution of **2a** (0.5 mmol) in THF (3 mL) was slowly added LiAlH_4 (1.2 mmol) at 0 °C under Ar atmosphere. Then, the whole was slowly warmed to room temperature for 12 hours. The reaction mixture was saturated aqueous NaHCO_3 and extracted with EtOAc. The organic layers dried over anhydrous sodium sulfate, and concentrated. The residue was purified by column chromatography on silica gel to the product **5a** in 78% yield.



3,4-dimethyl-2,5-diphenyl-1H-pyrrole (5a). ^1H NMR (400 MHz, CDCl_3): δ 7.99 (br, 1H), 7.38-7.47 (m, 8H), 7.22-7.24 (m, 2H), 2.22 (s, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 133.8, 128.9, 128.8, 126.8, 126.3, 117.6, 10.6. HRMS (ESI): m/z : calcd for $\text{C}_{18}\text{H}_{18}\text{N}$ $[\text{M} + \text{H}]^+$ 248.1439, found: 248.1440.



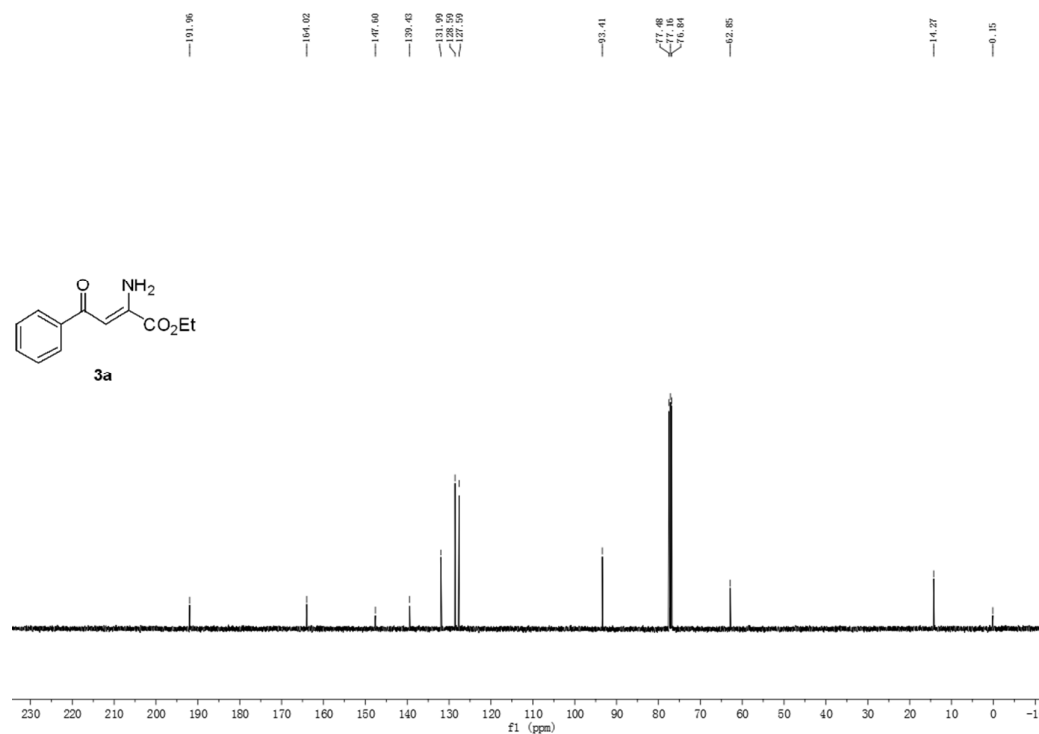
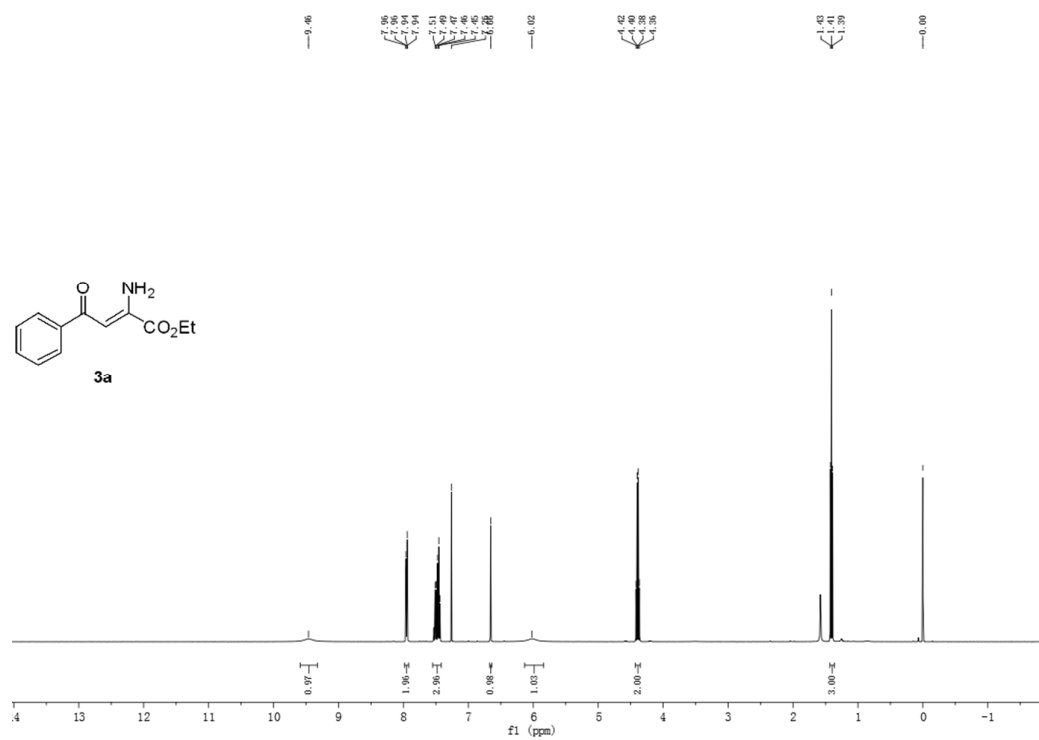
$\text{Pd(PPh}_3)_2\text{Cl}_2$ (0.03 mmol) was added to a solution of **2j** (0.3 mmol), 4-methylphenylboronic acid (2 mmol) and Na_2CO_3 (3 mmol) in DMF (5 mL) under argon at room temperature. The mixture was heated to 100 °C, and stirred overnight. The resulting mixture was then quenched with water (10 mL), and extracted with EtOAc (2 x 10 mL). The combined organic layers were washed with brine (2 x 10 mL), dried over anhydrous sodium sulfate and concentrated. The residue was purified by column chromatography on silica gel to afford the product **6a** in 95% yield.

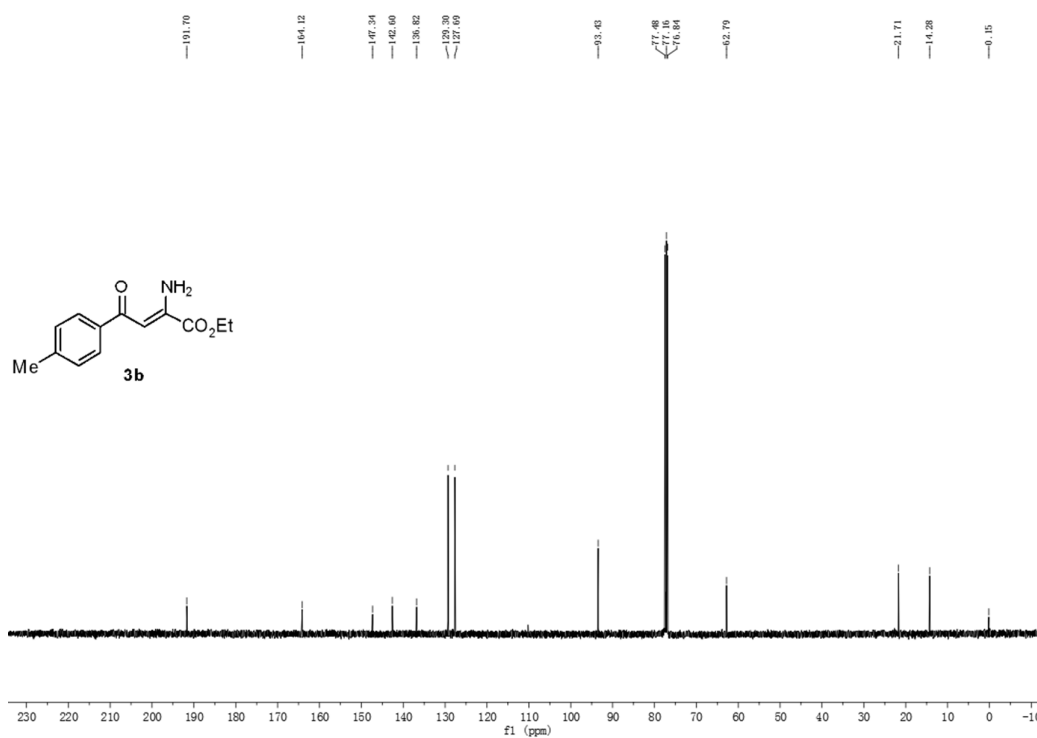
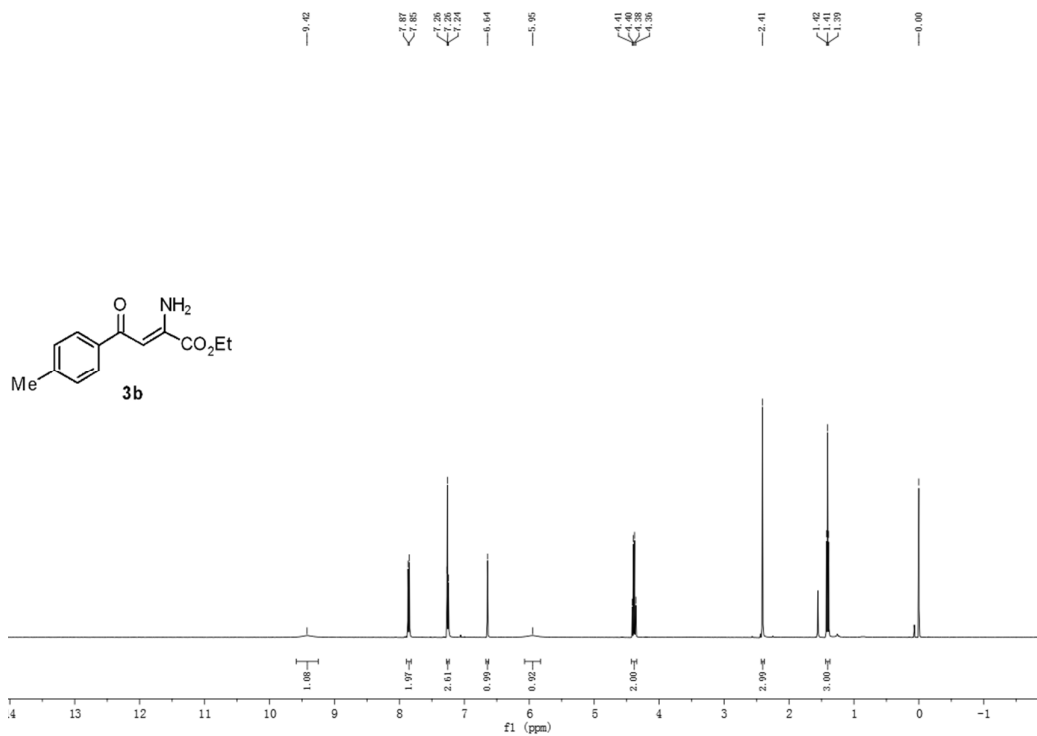


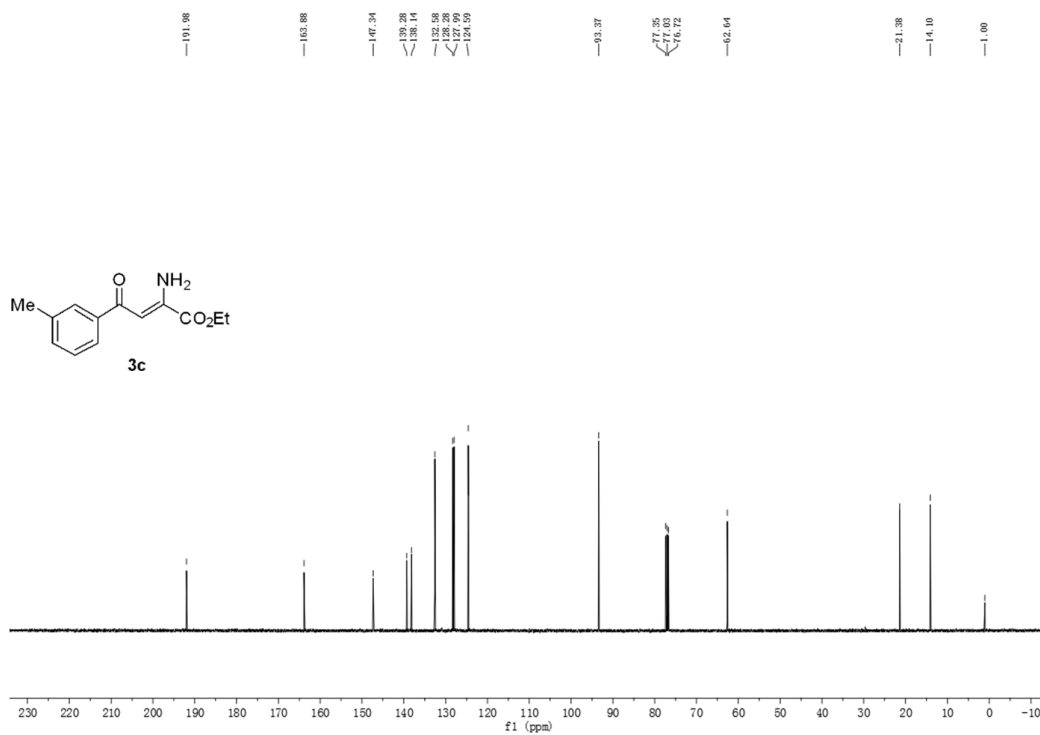
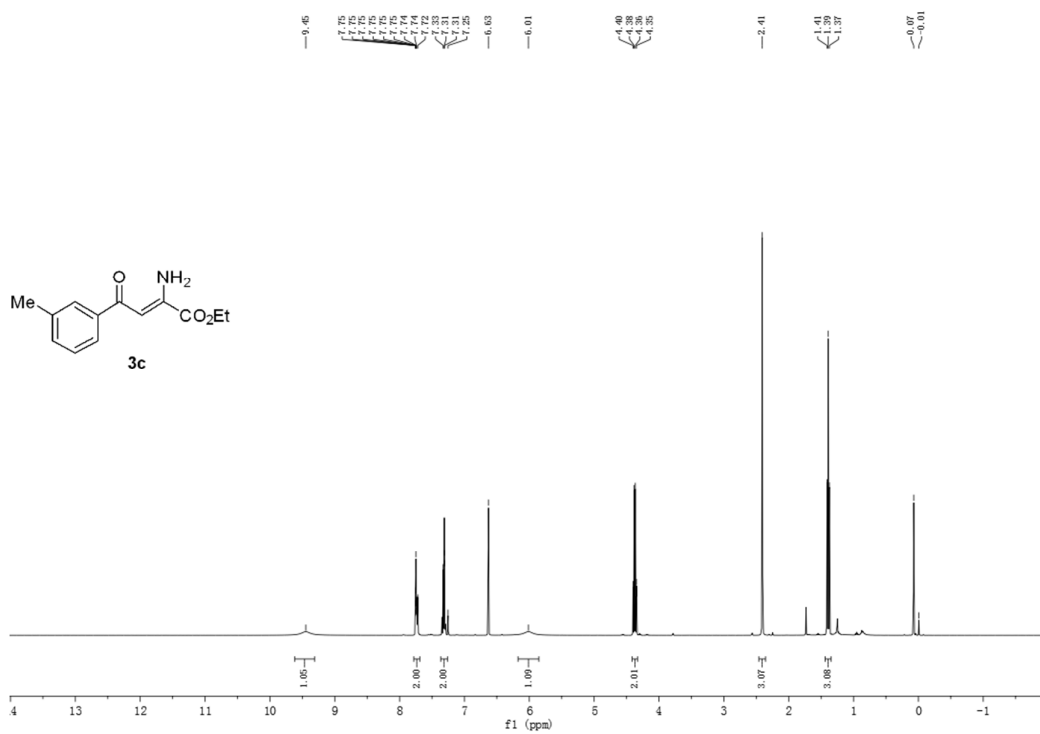
Dimethyl 2,5-bis(4'-methyl-[1,1'-biphenyl]-4-yl)-1H-pyrrole-3,4-dicarboxylate (6a).

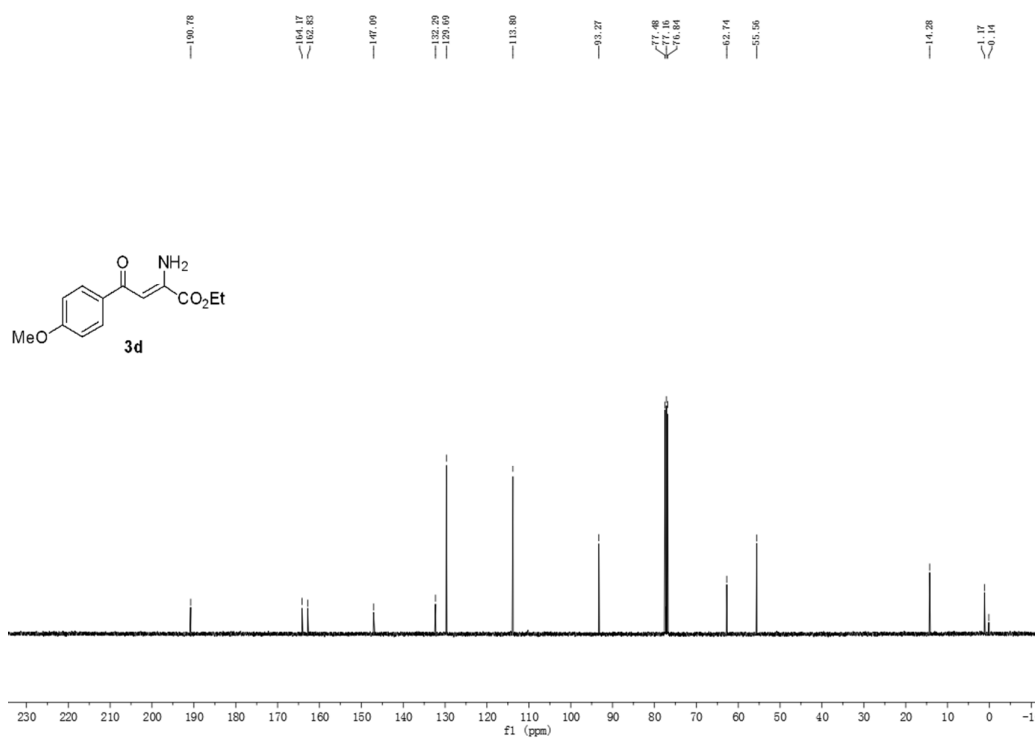
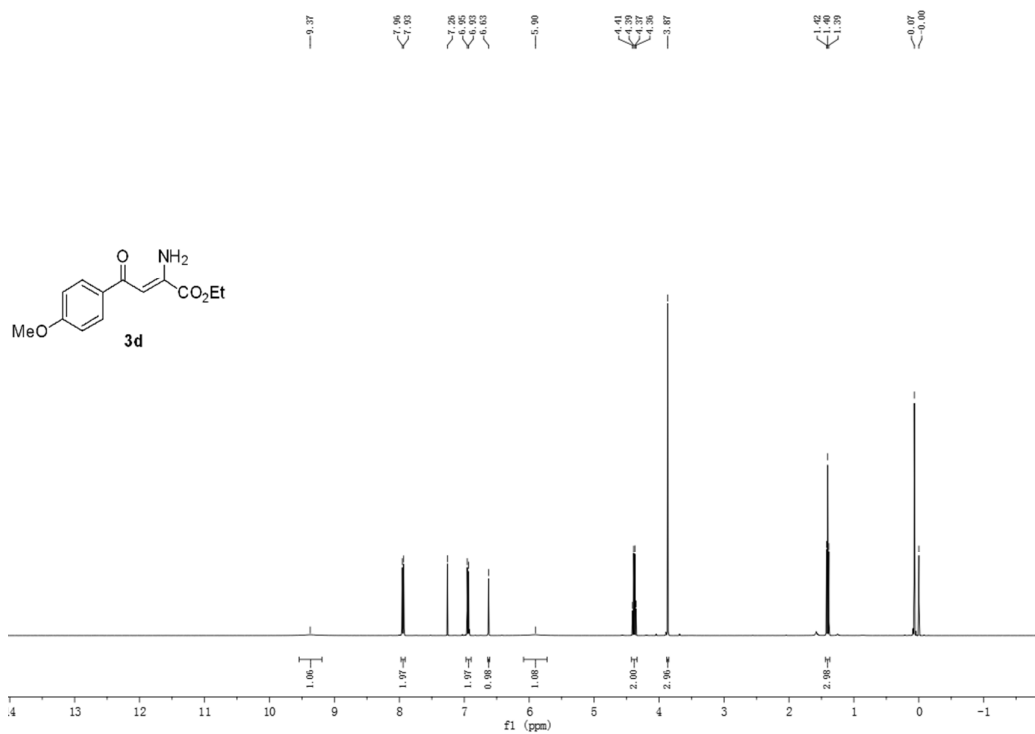
^1H NMR (400 MHz, CDCl_3): δ 8.56 (br, 1H), 7.62 (s, 8H), 7.50 (d, J = 8.0 Hz, 4H), 7.19-7.24 (m, 4H), 3.80 (s, 6H), 2.39 (s, 6H). ^{13}C NMR (100 MHz, CDCl_3): δ 165.9, 141.5, 137.7, 137.5, 134.4, 129.8, 129.5, 128.5, 127.3, 127.0, 114.5, 52.1, 21.3. HRMS (ESI): m/z : calcd for $\text{C}_{34}\text{H}_{29}\text{NNaO}_4$ $[\text{M} + \text{Na}]^+$ 538.1994, found: 538.1993.

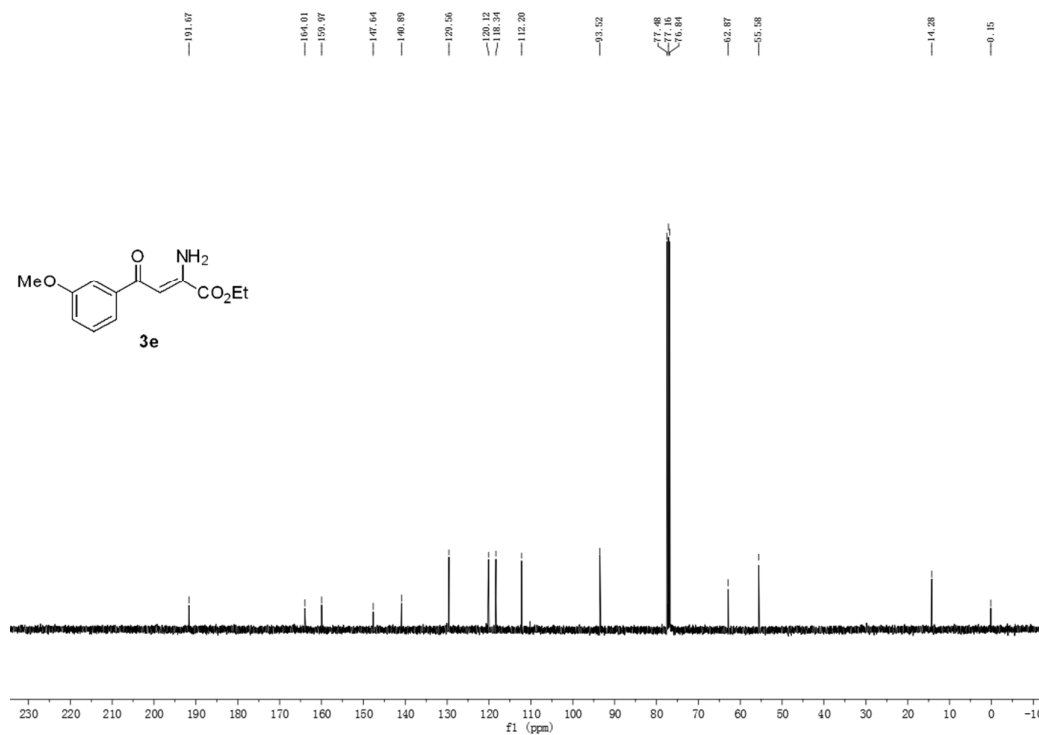
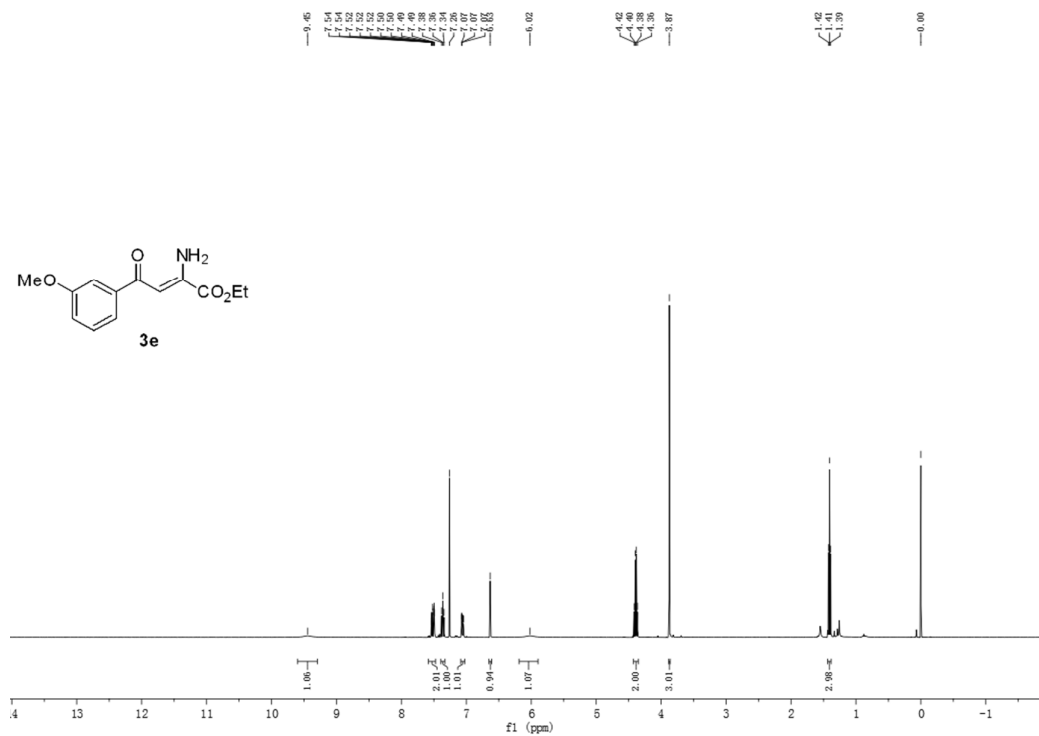
4. ^1H NMR and ^{13}C NMR spectra

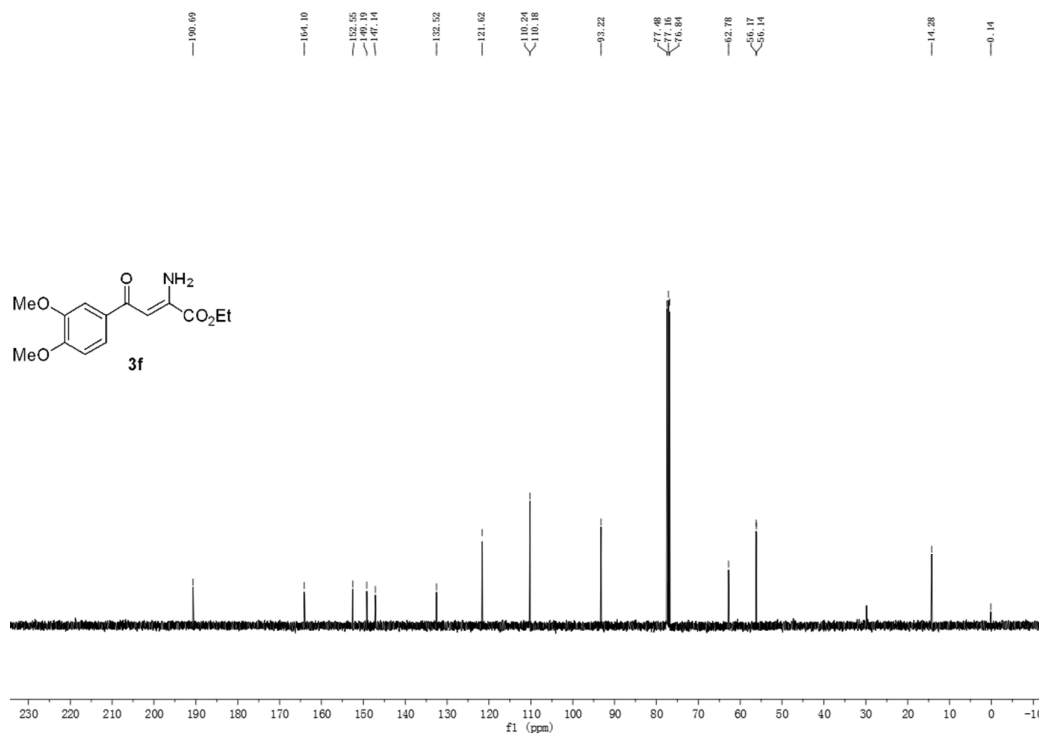
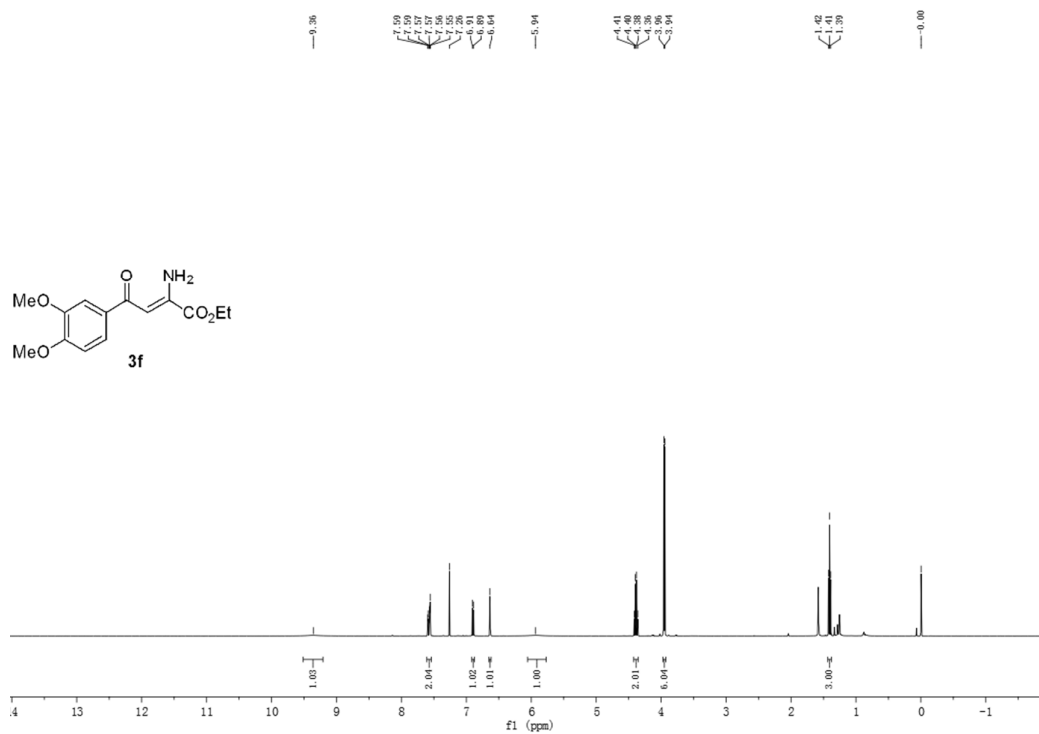


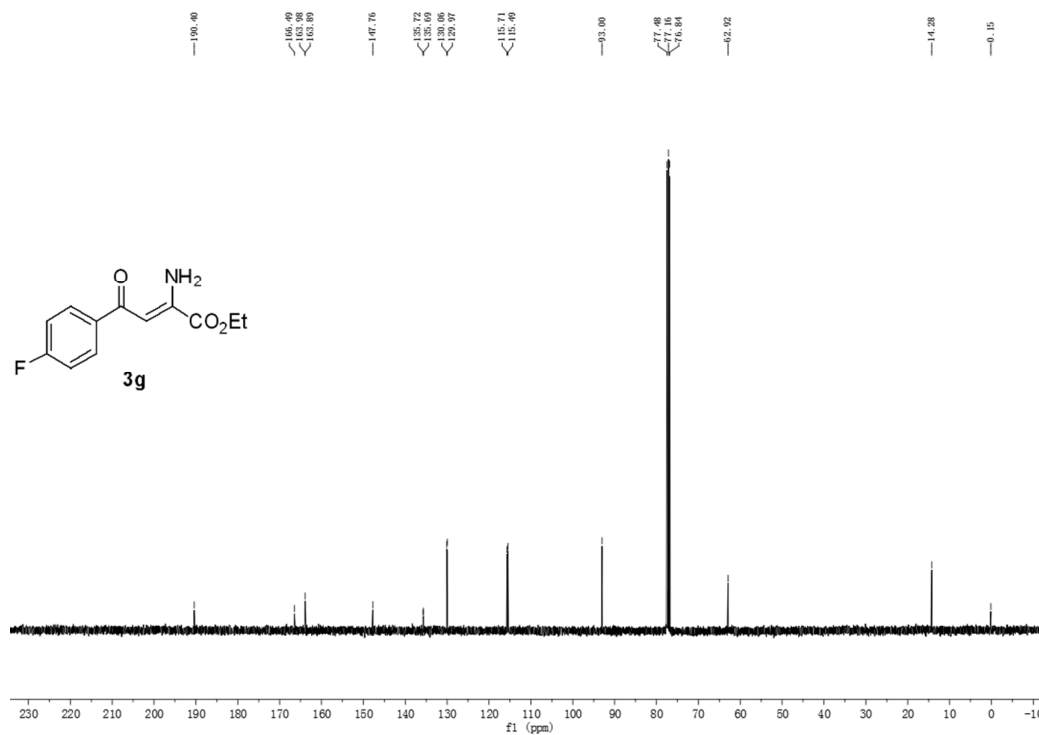
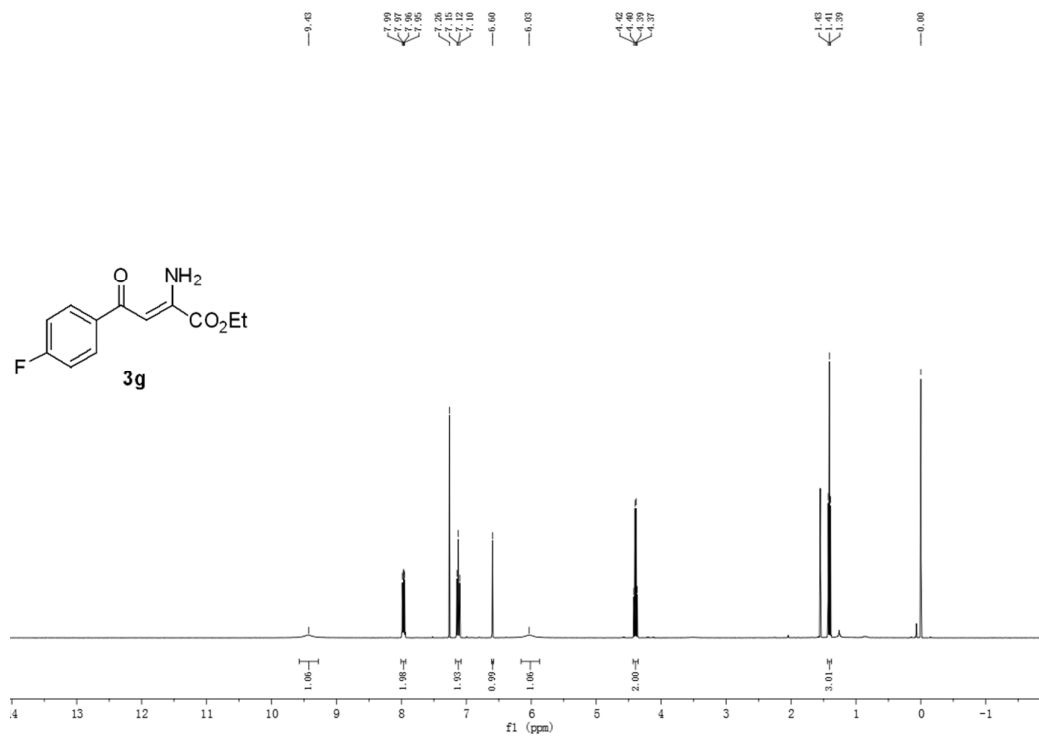


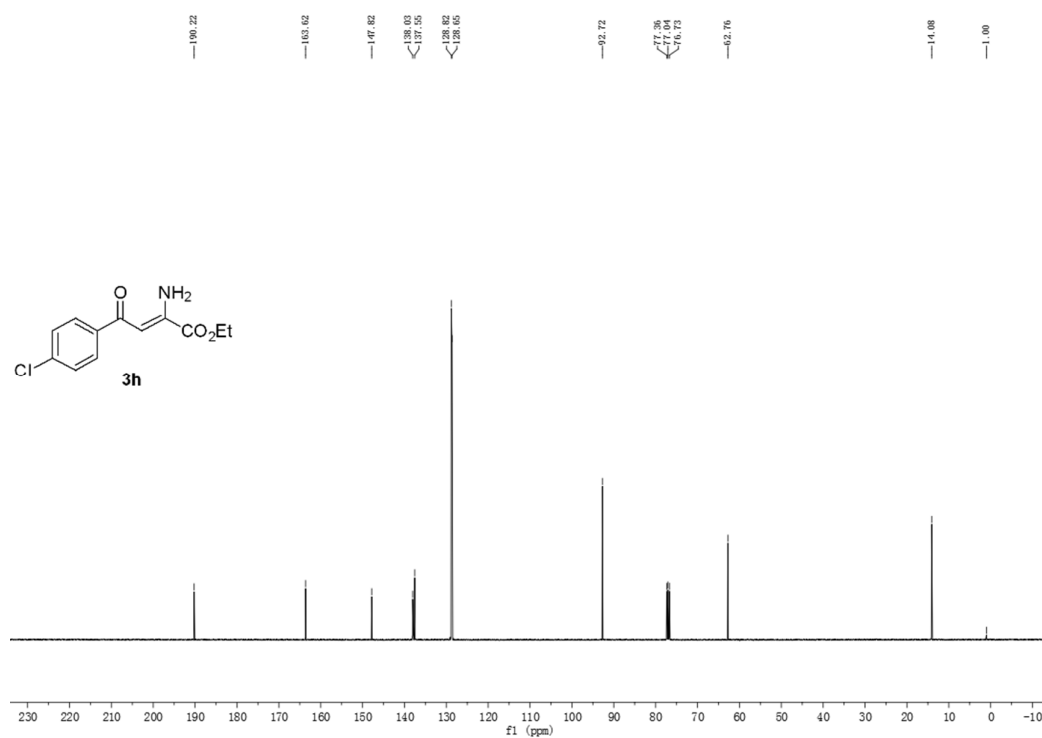
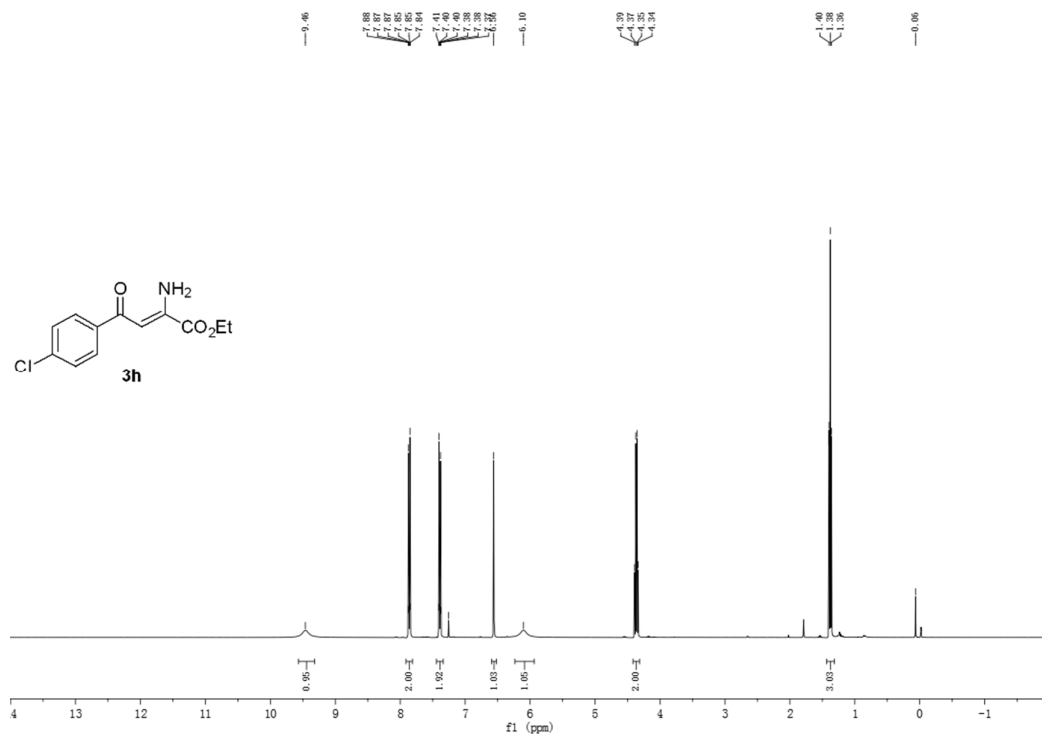


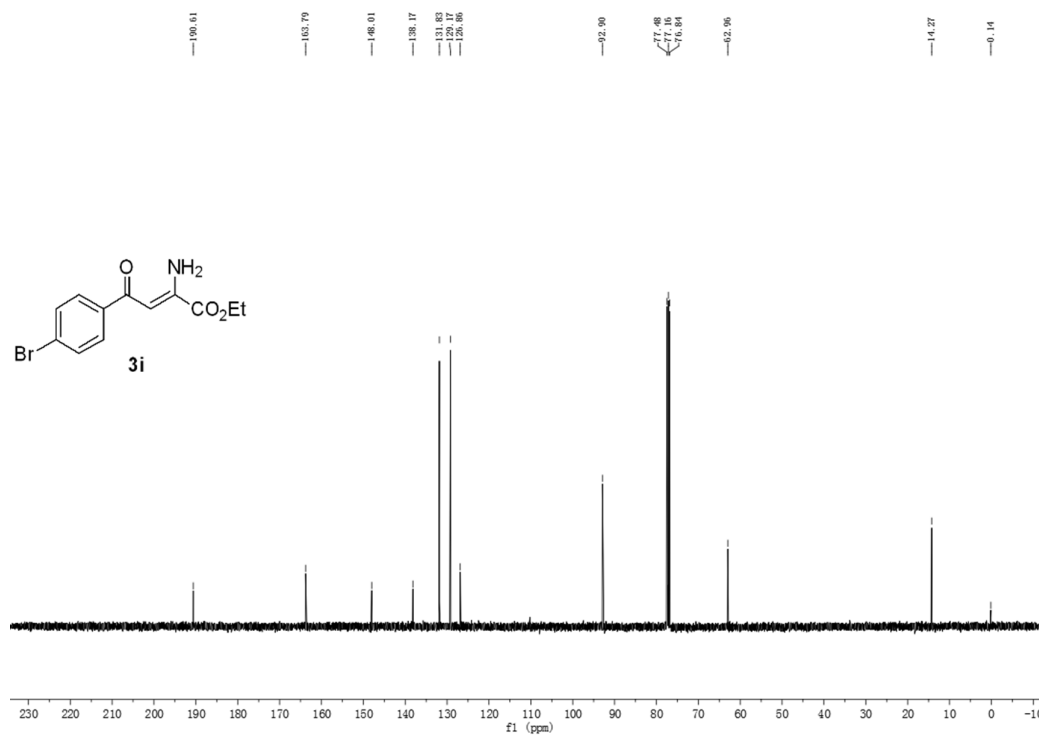
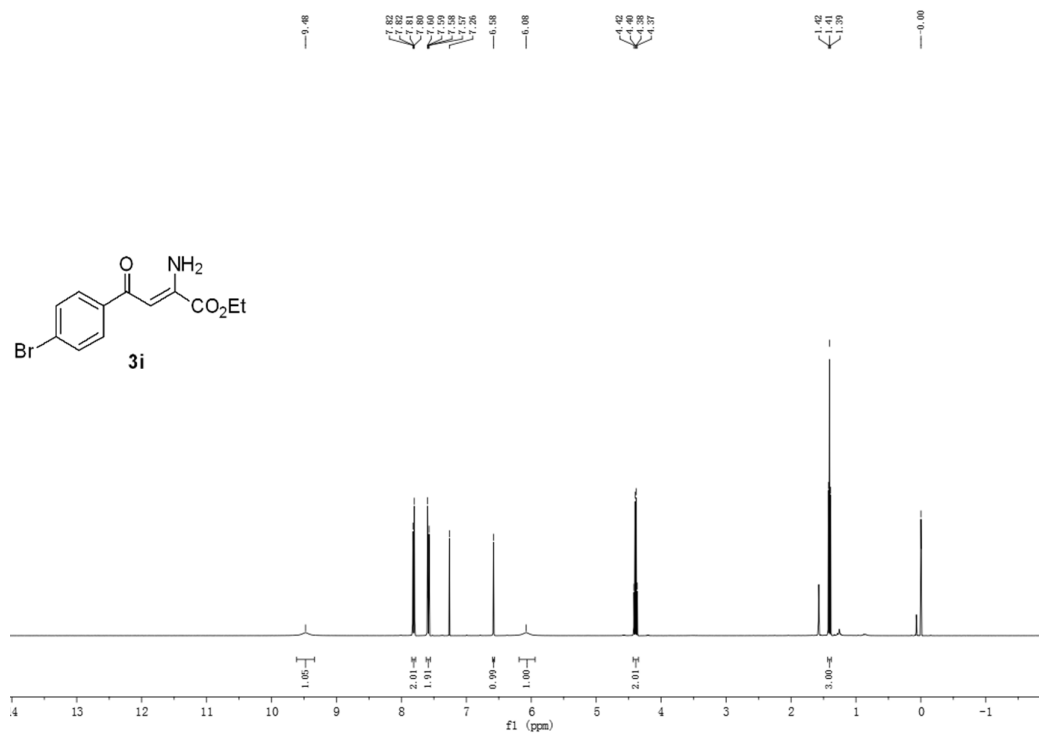


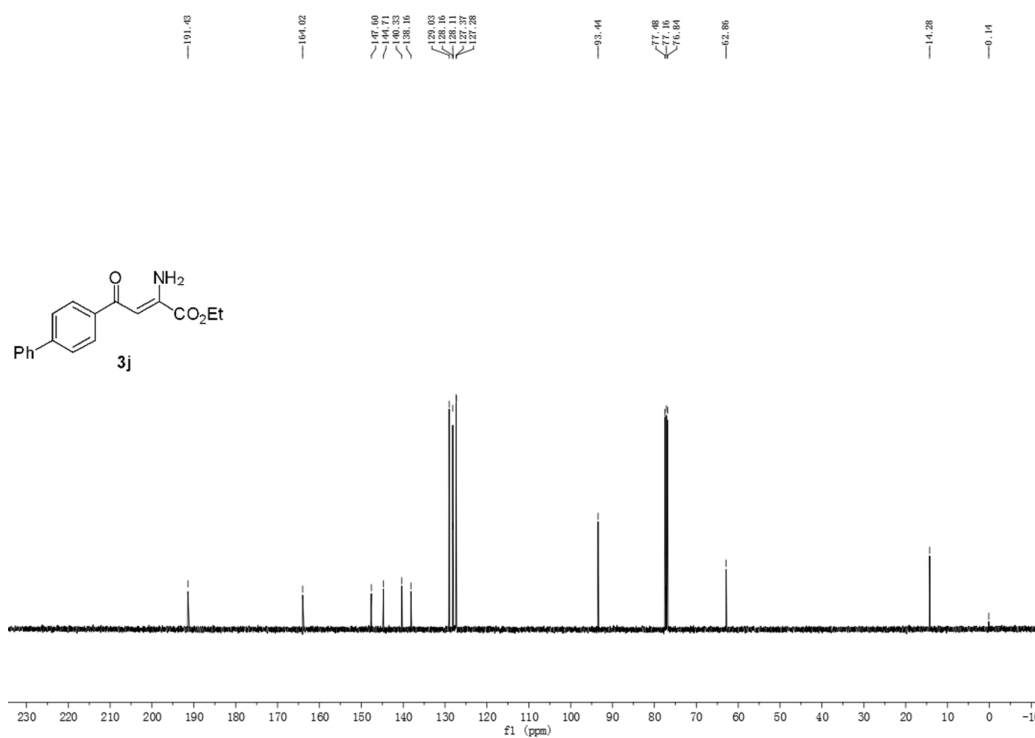
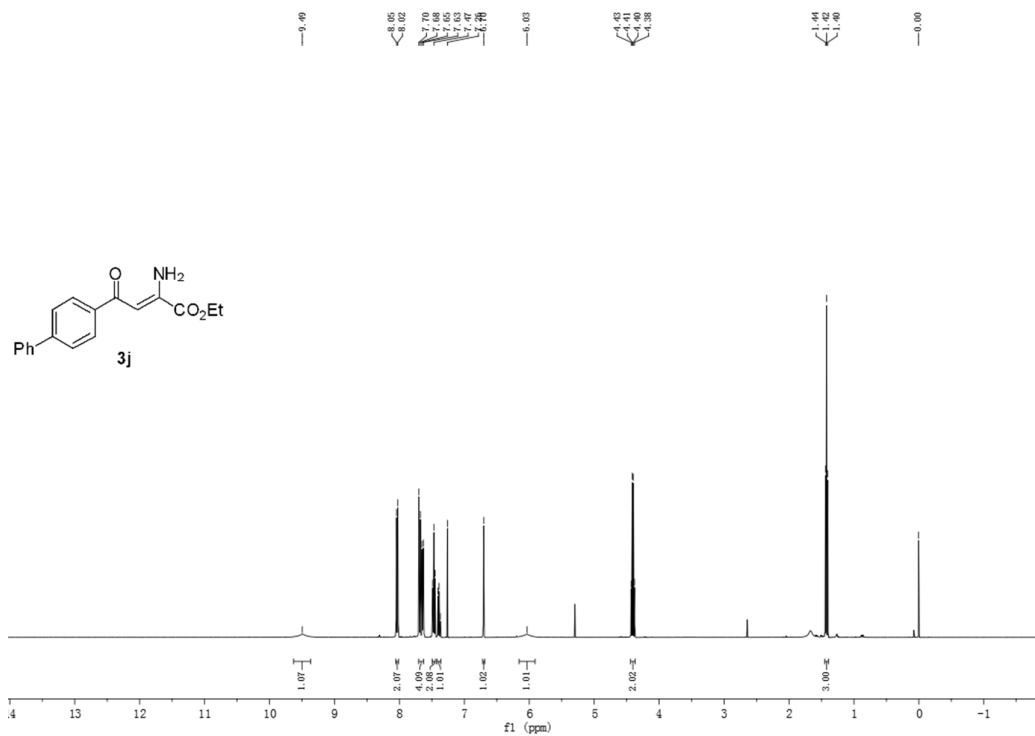


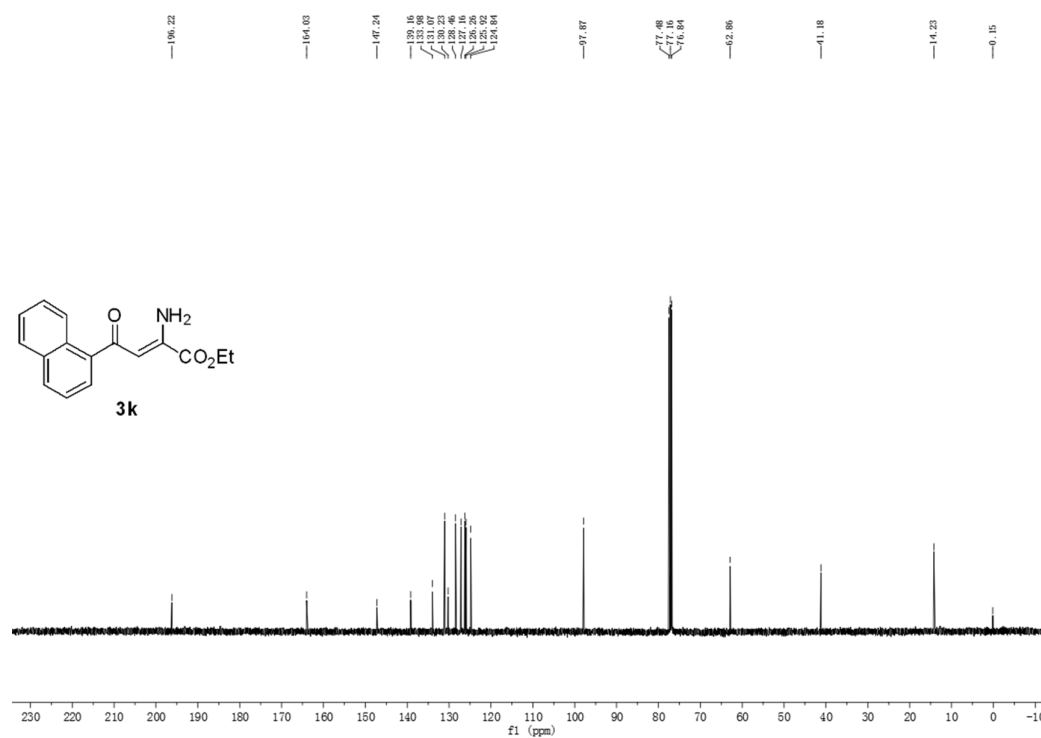
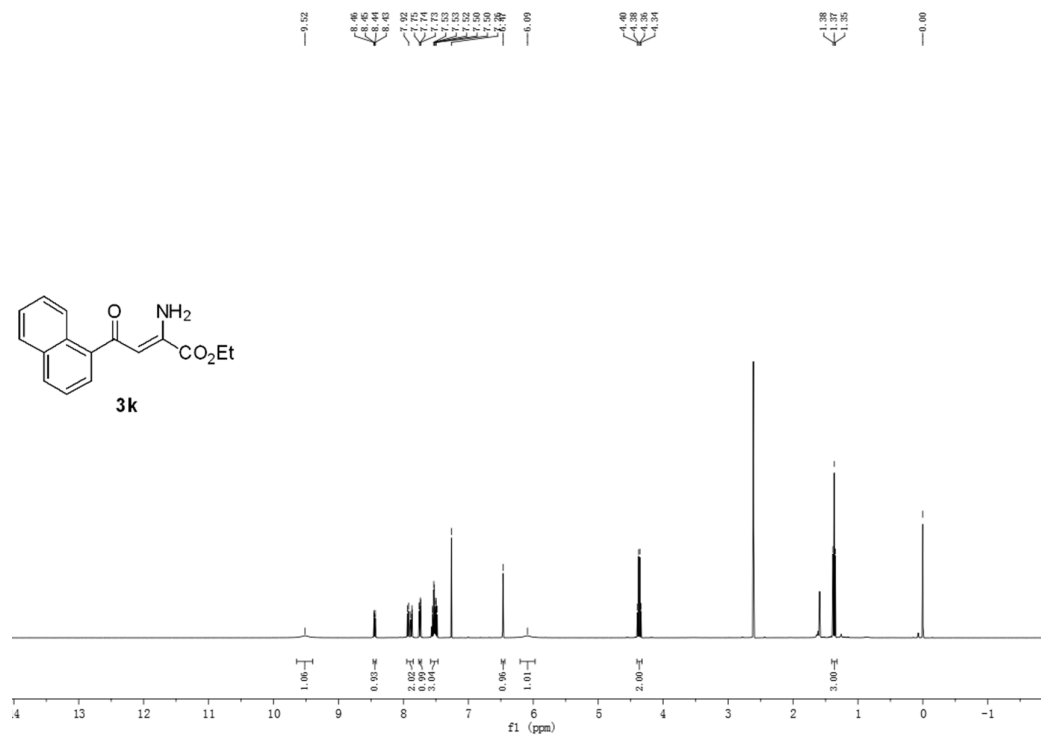


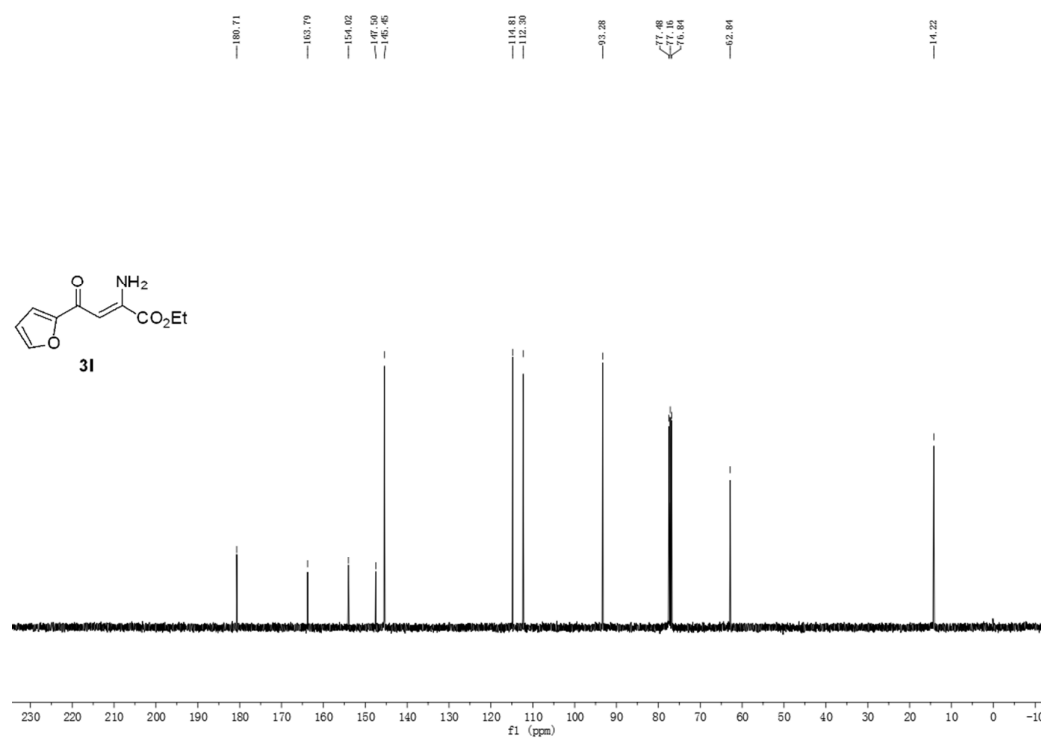
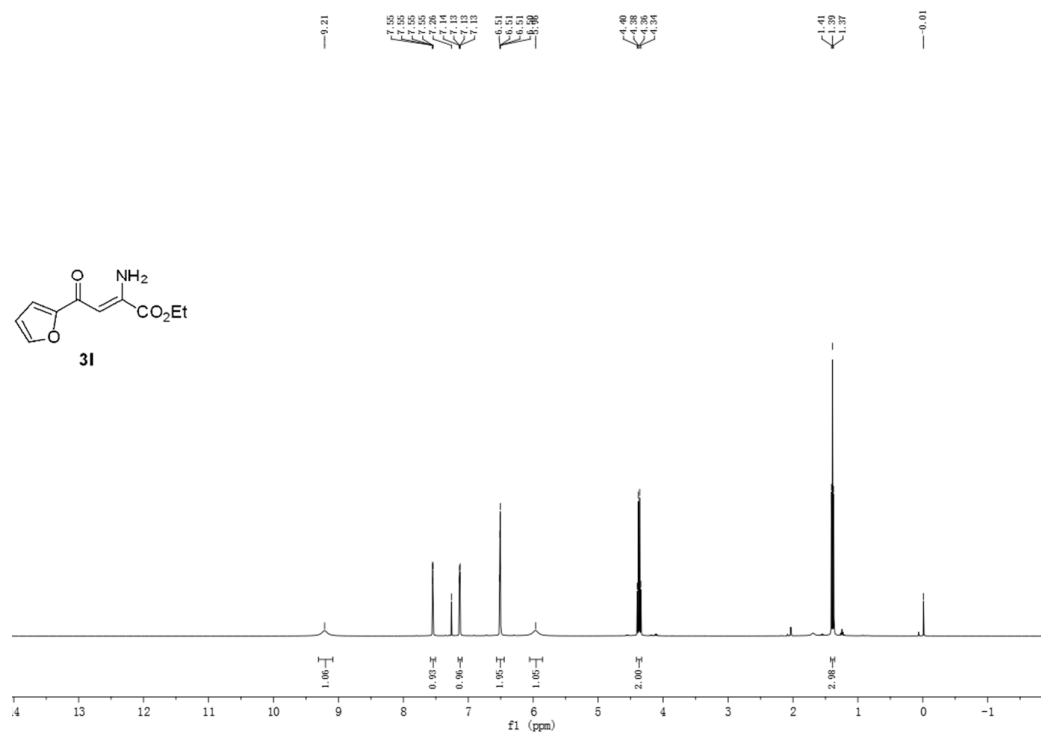


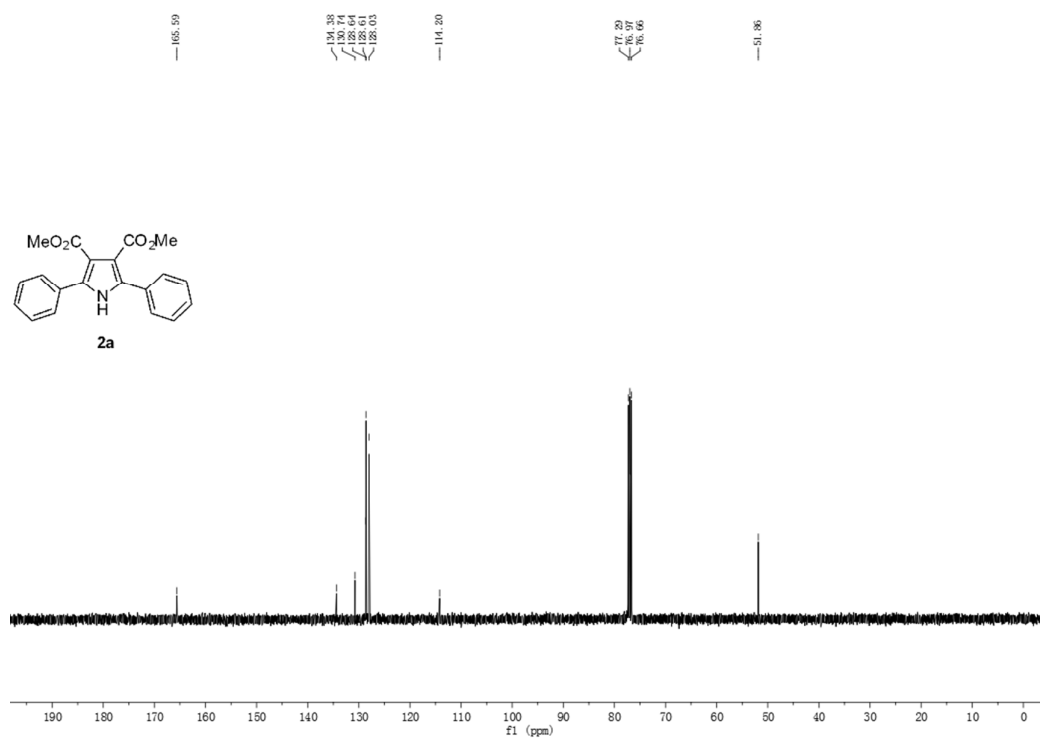
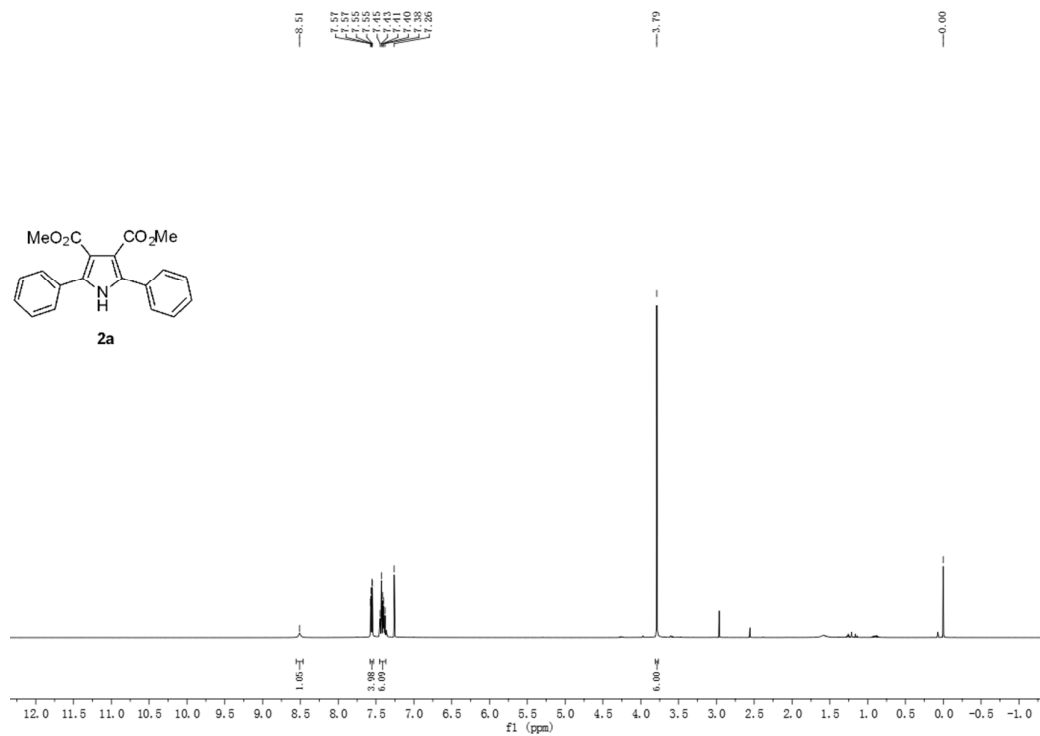


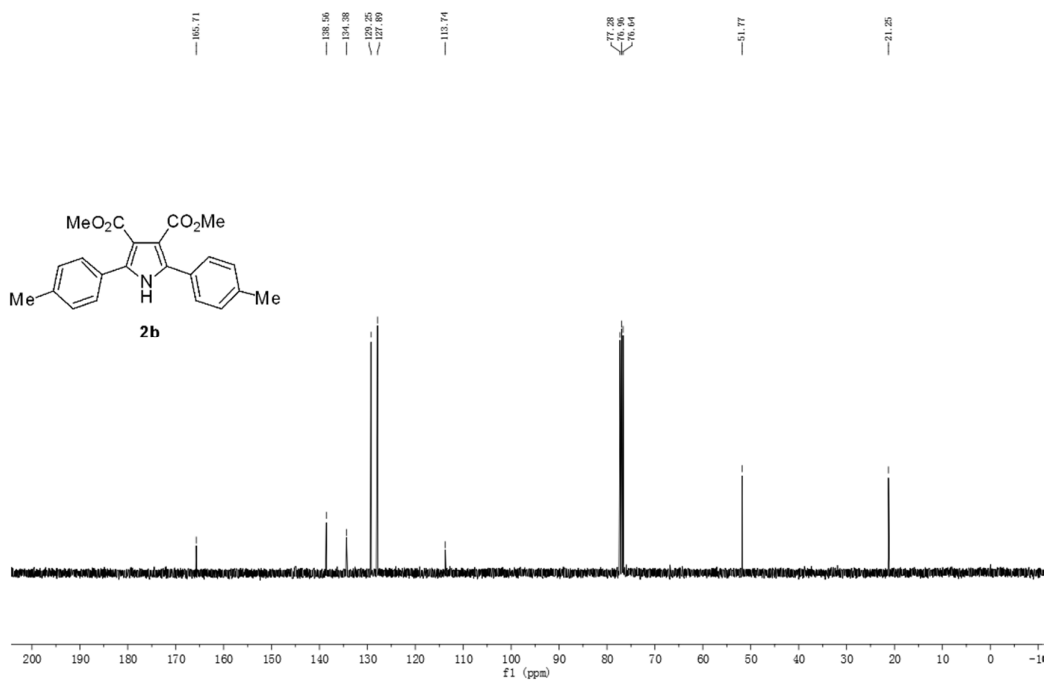
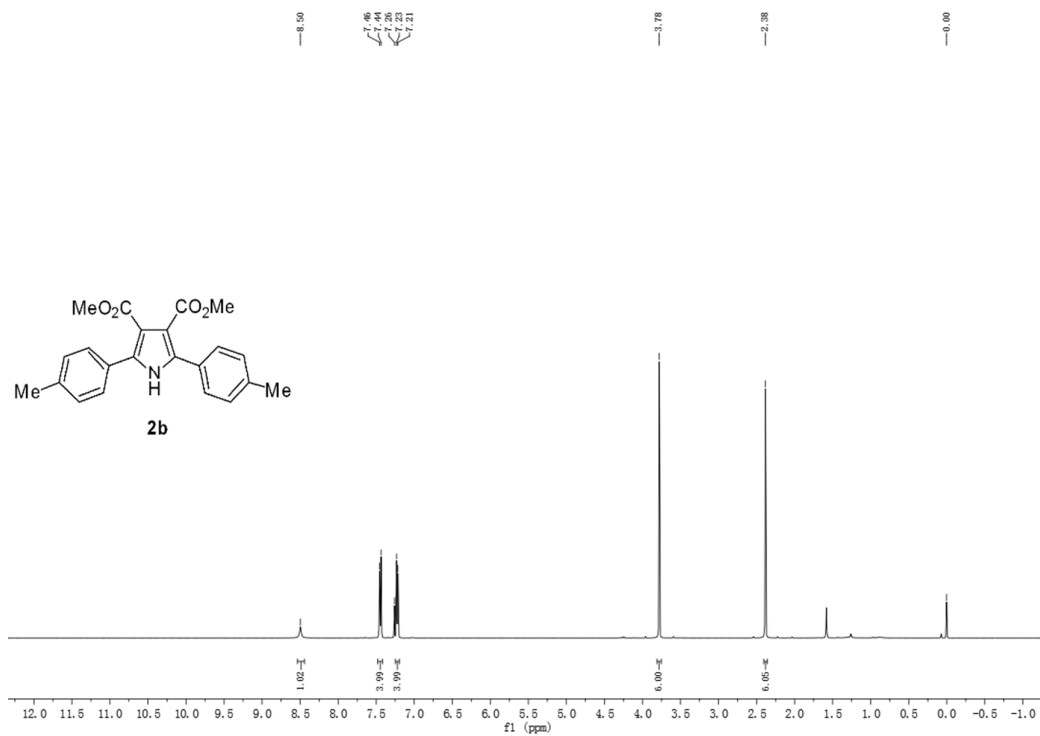


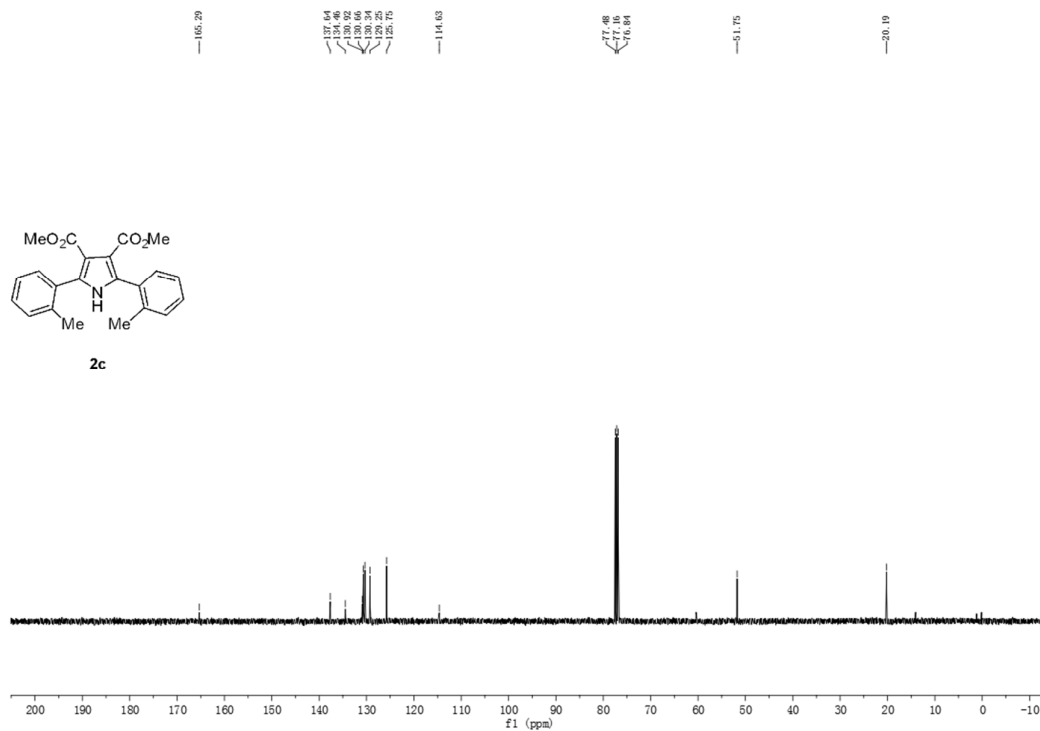
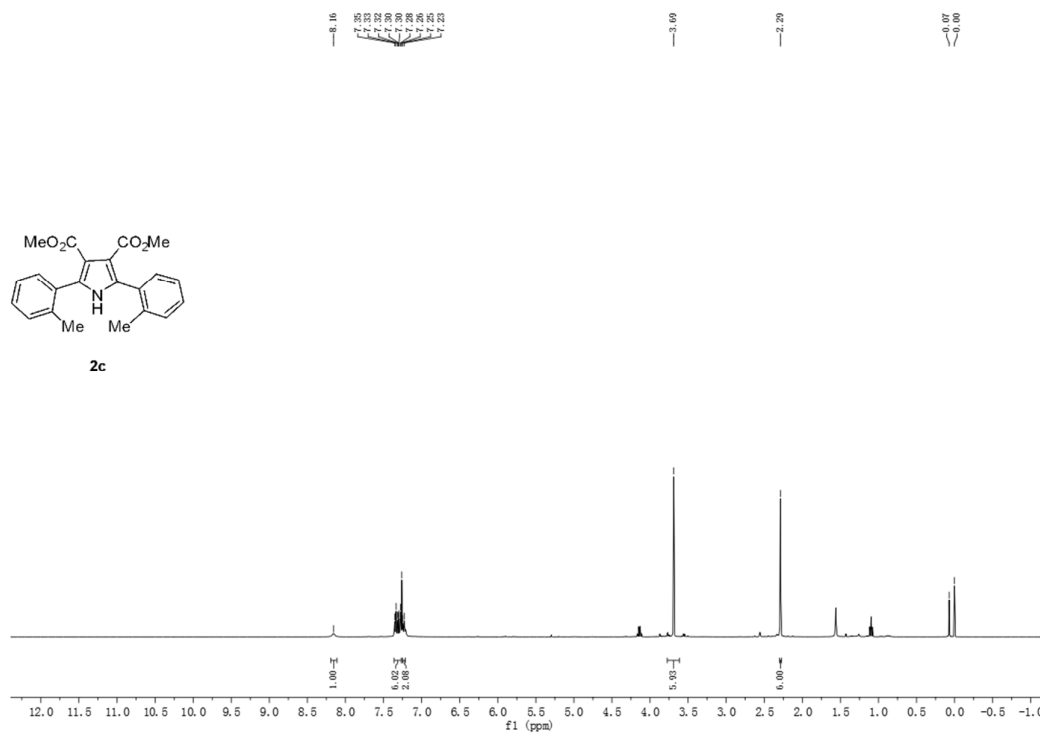


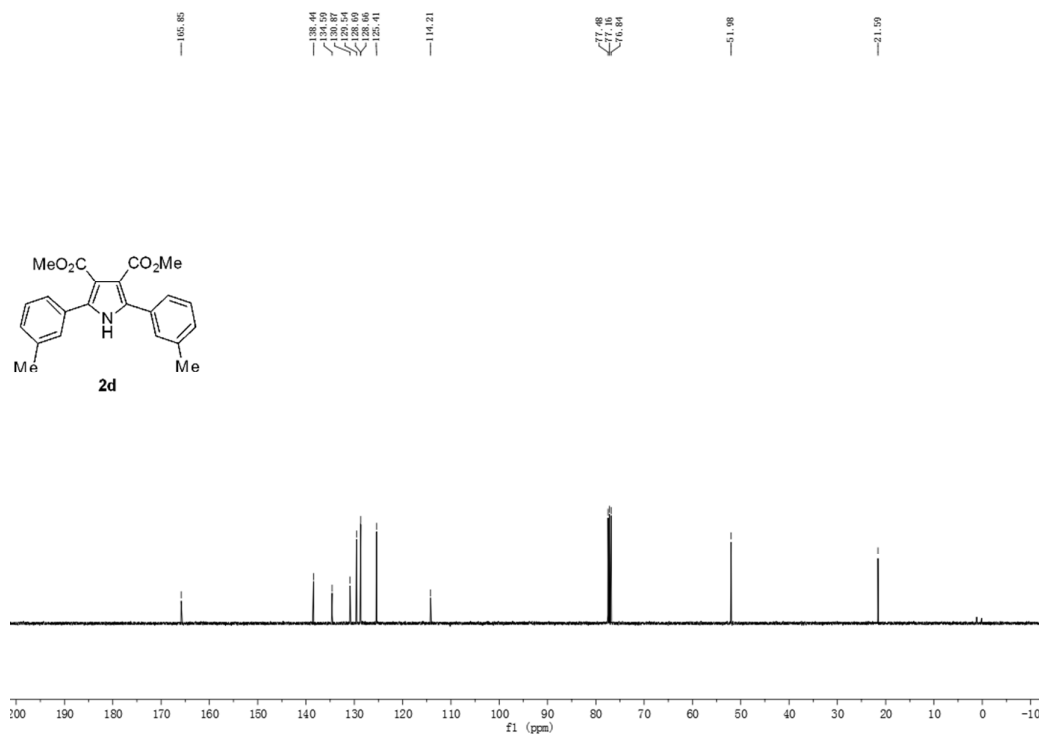
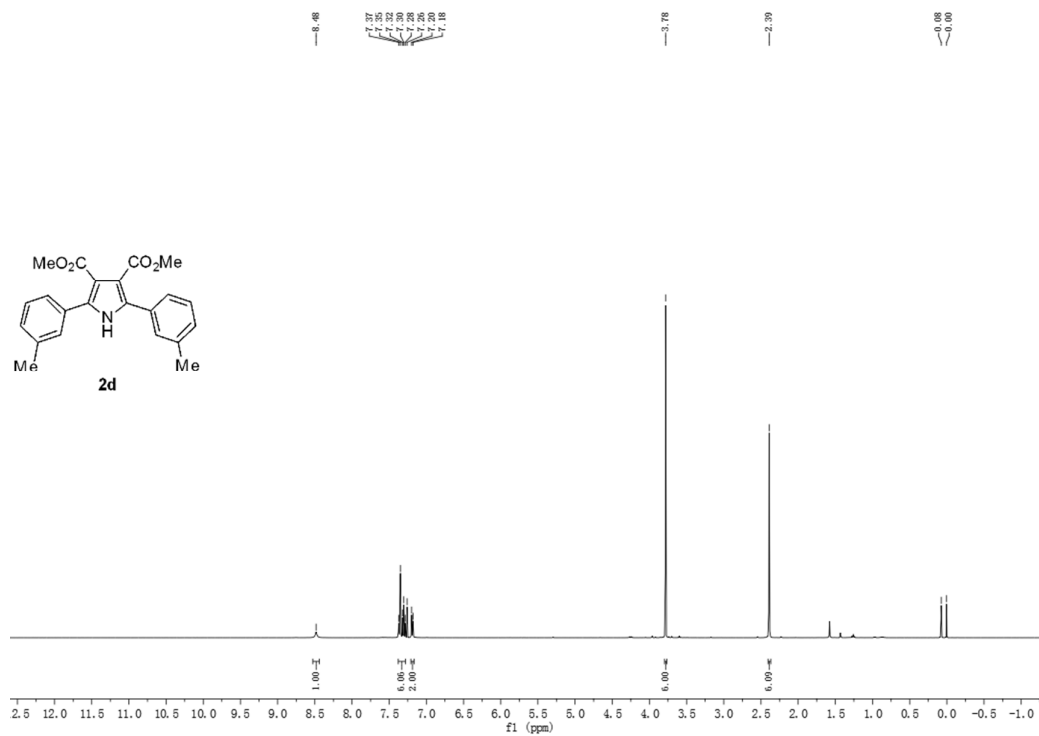


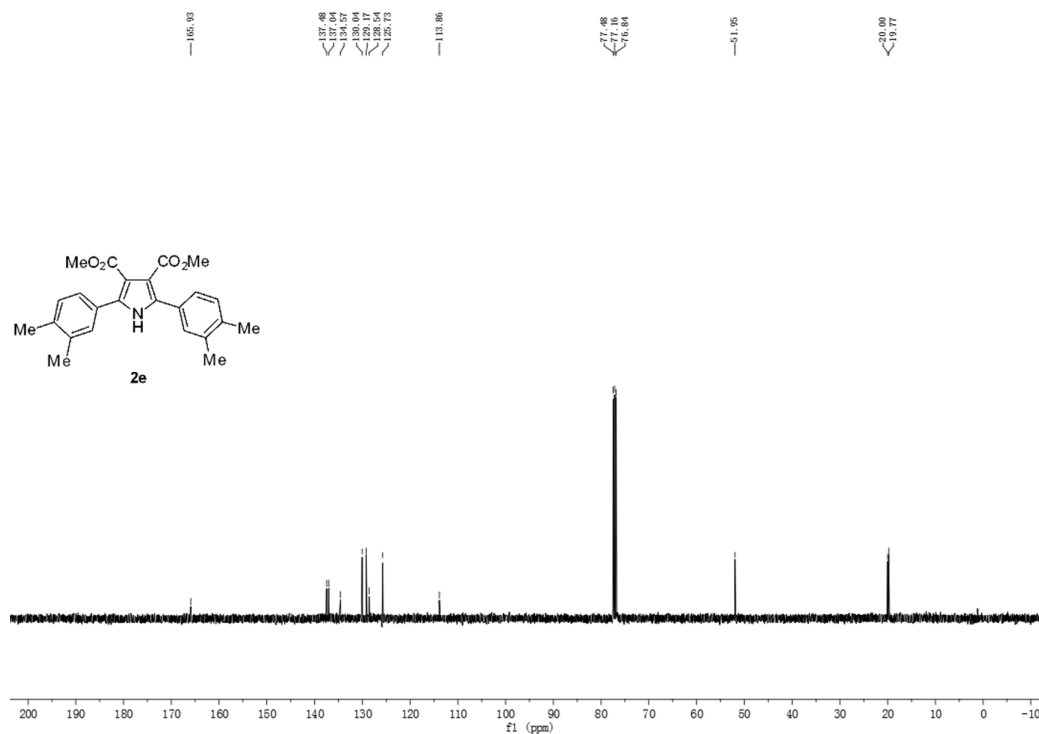
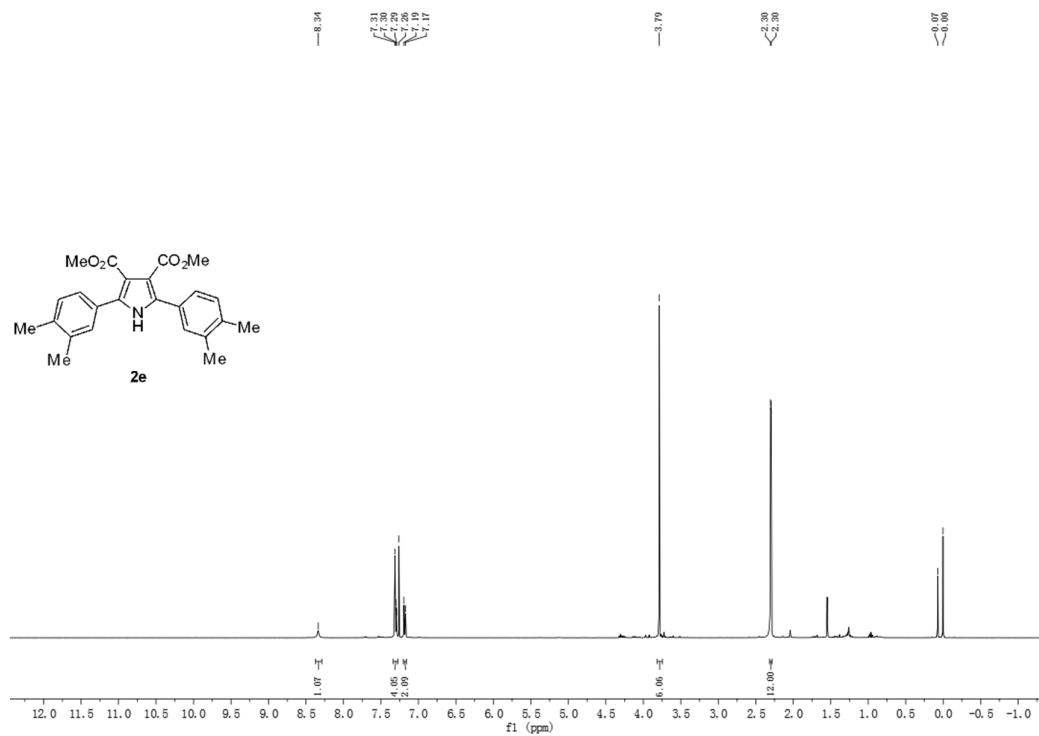


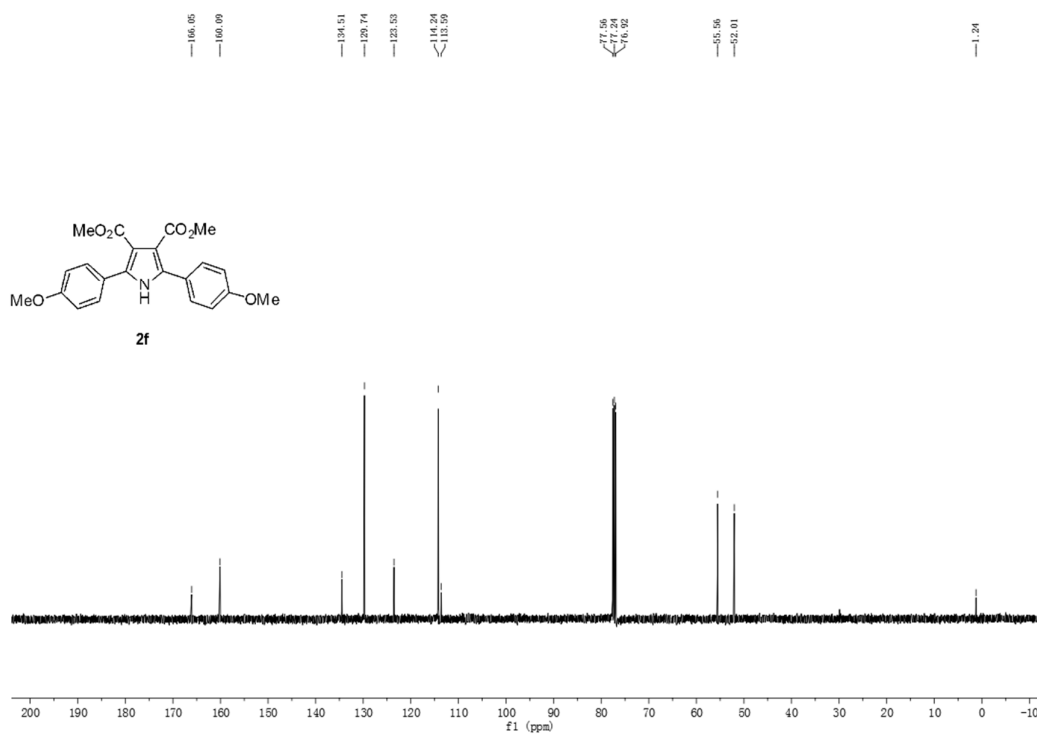
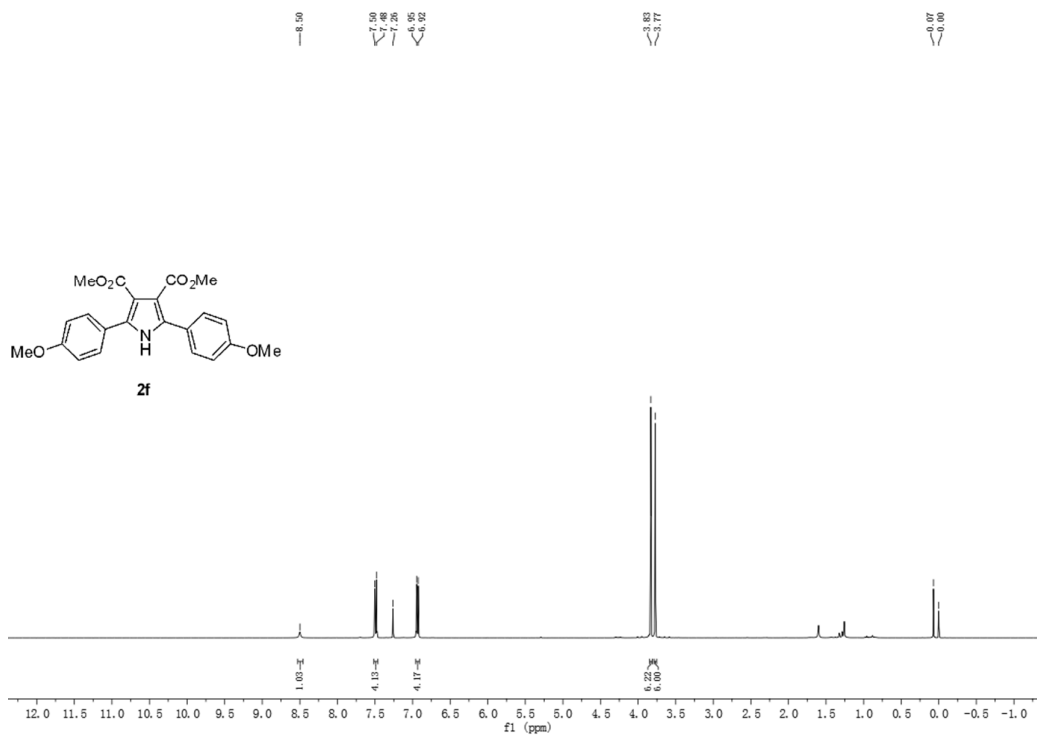


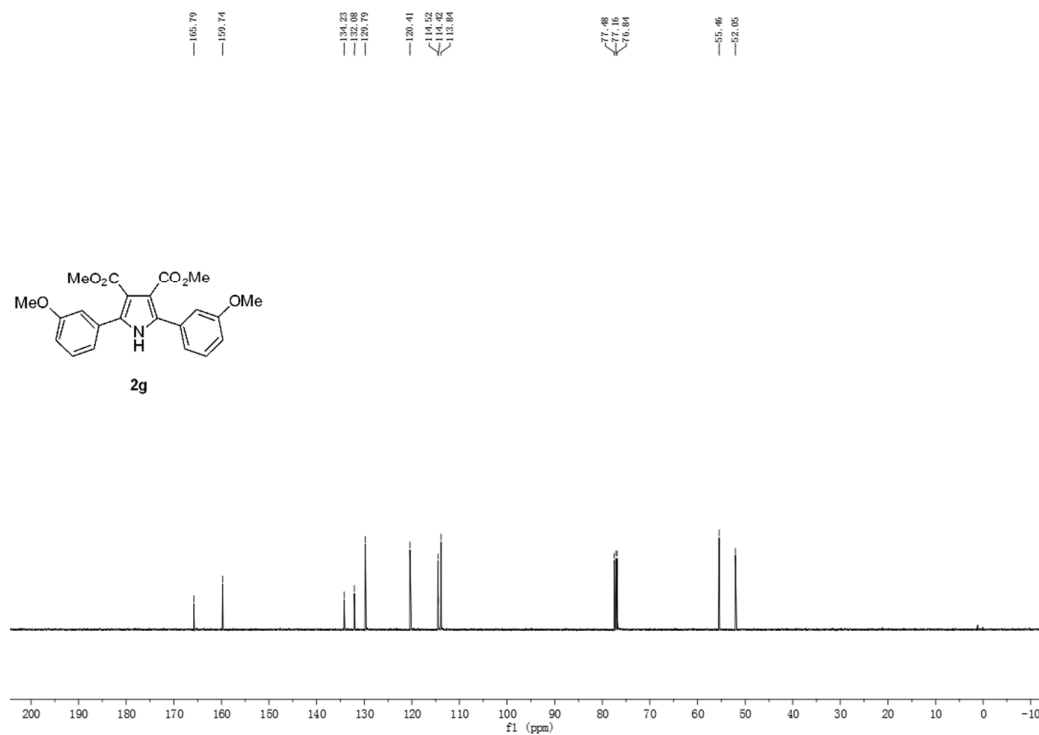
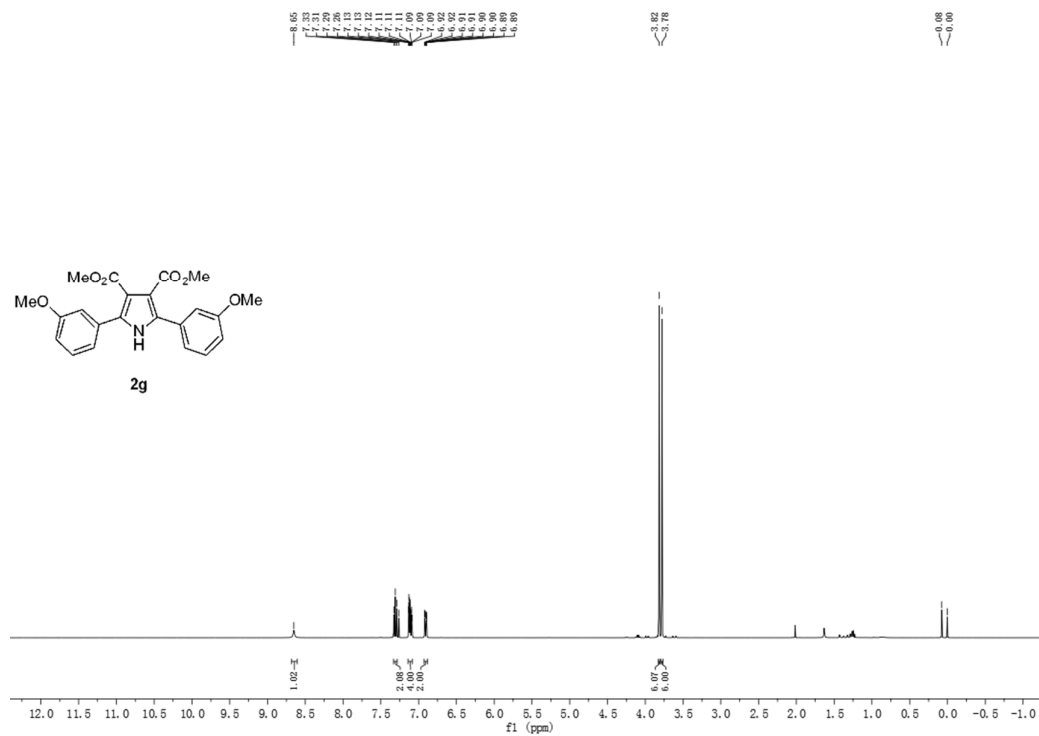


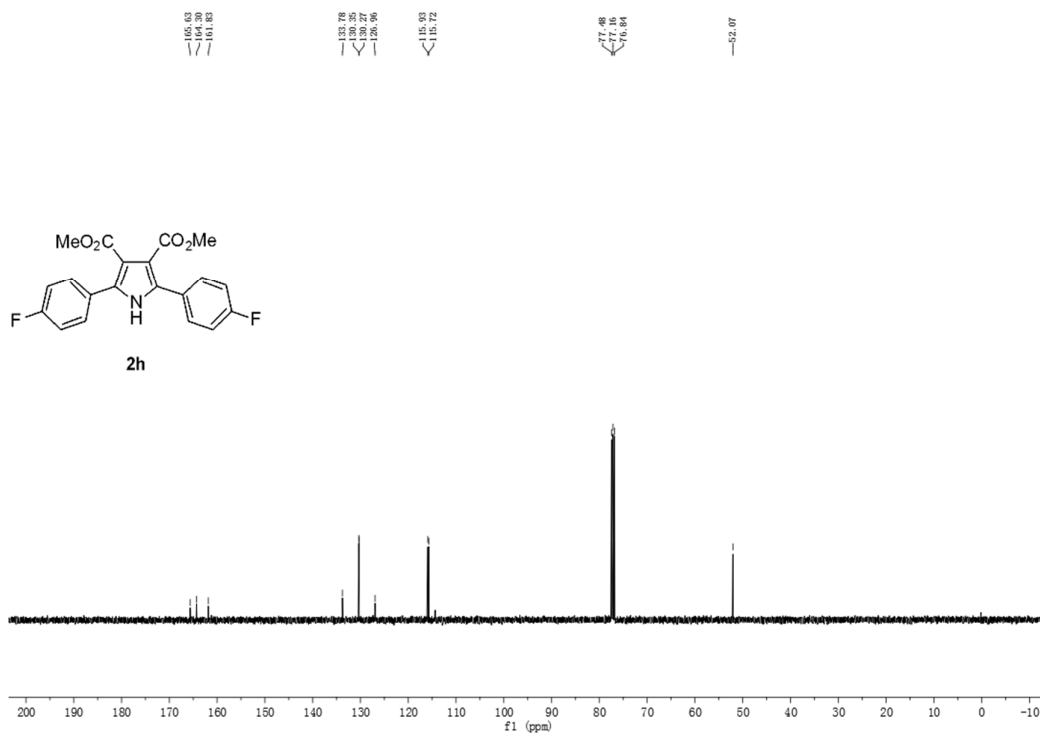
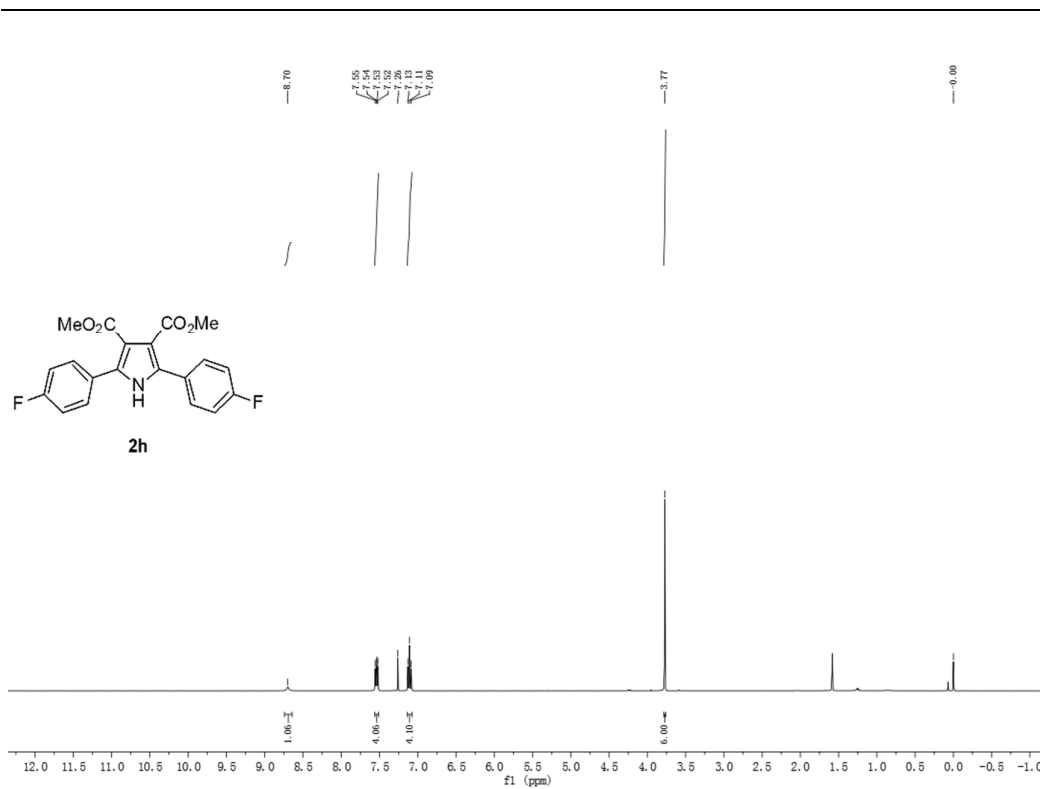


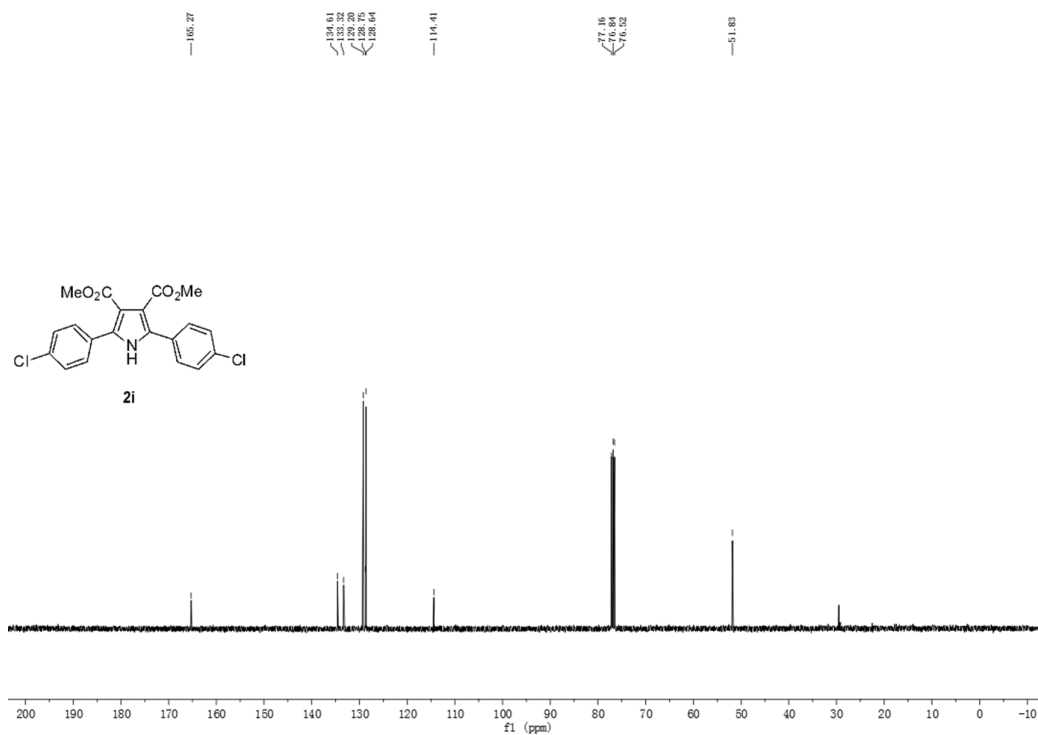
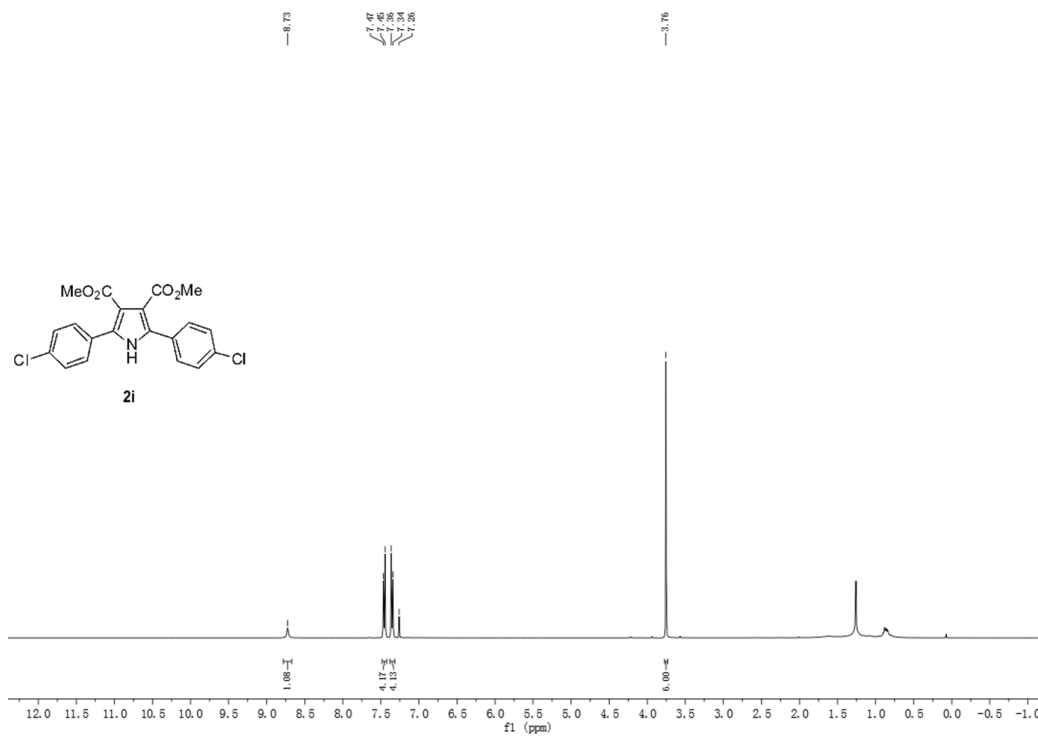


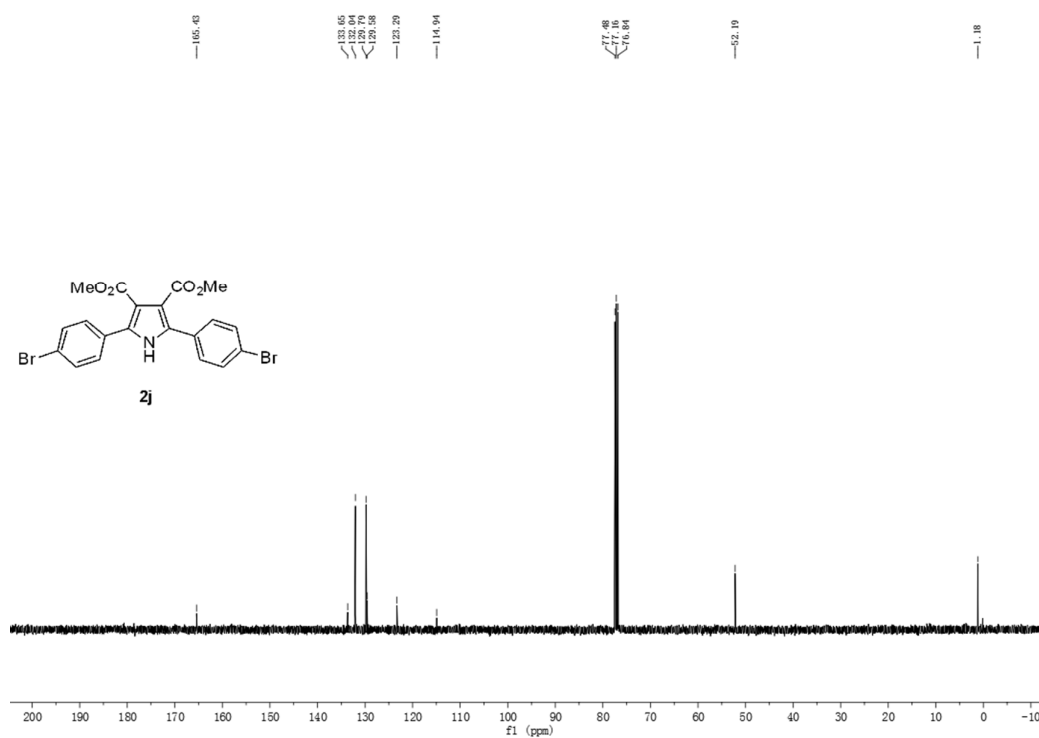
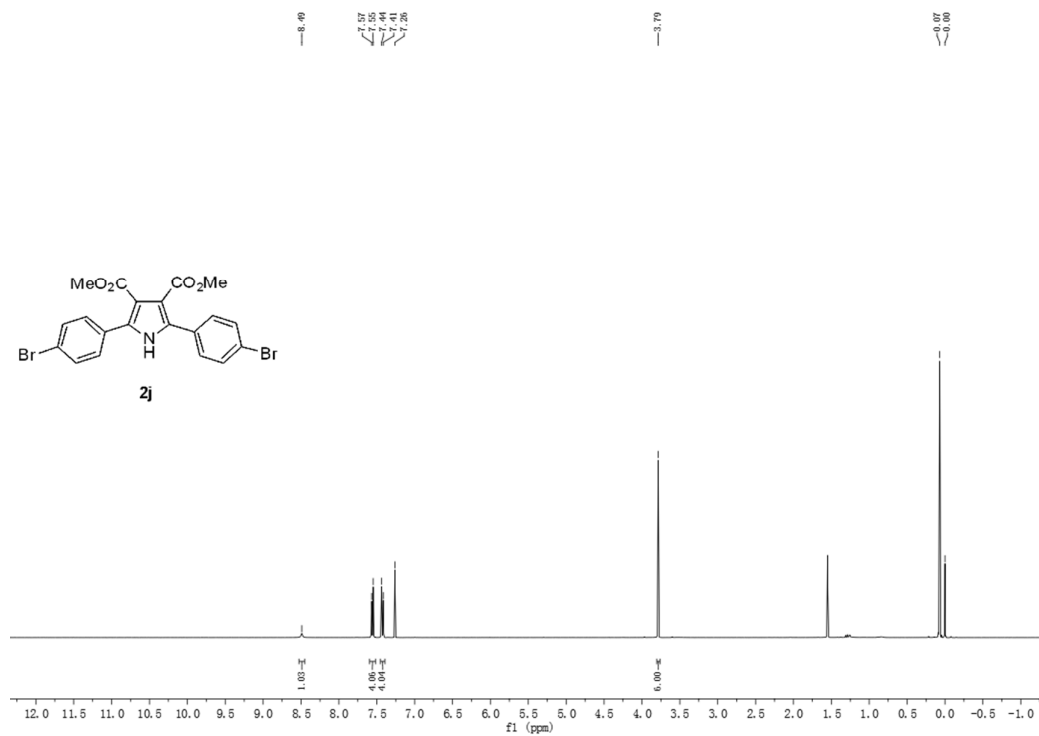


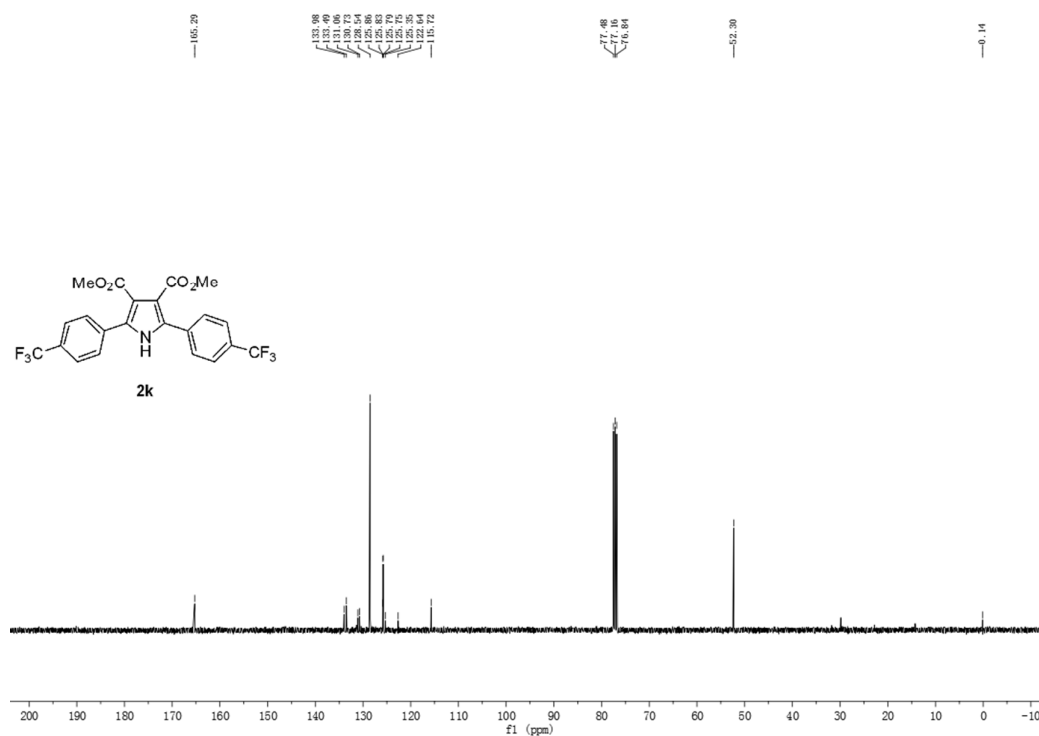
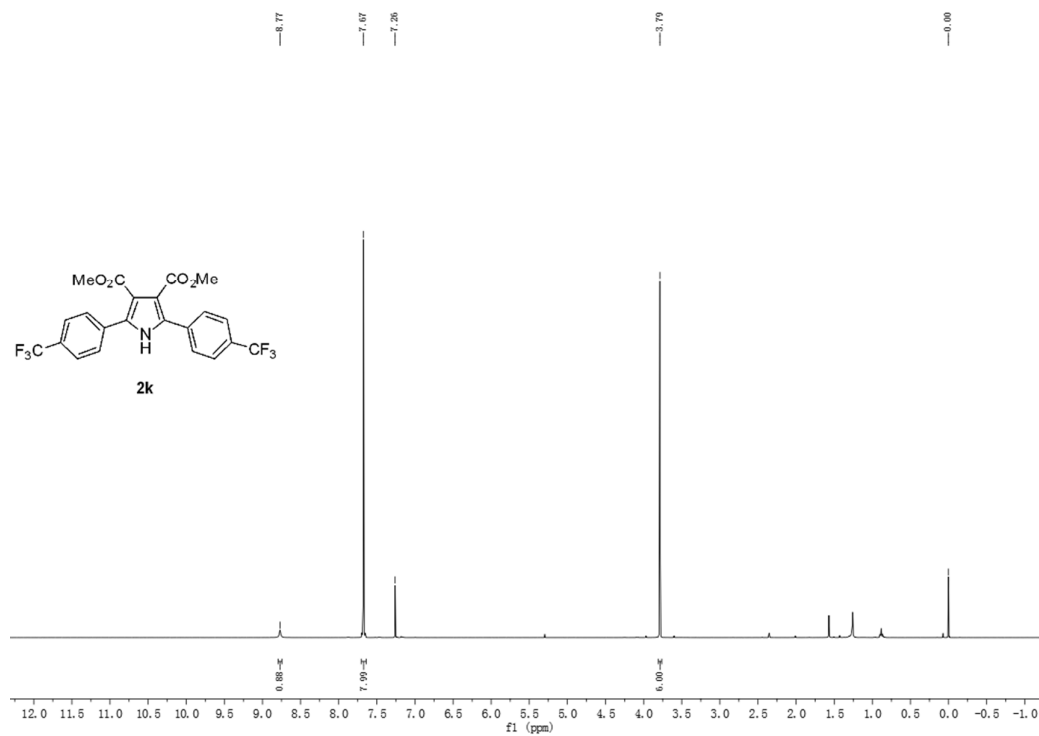


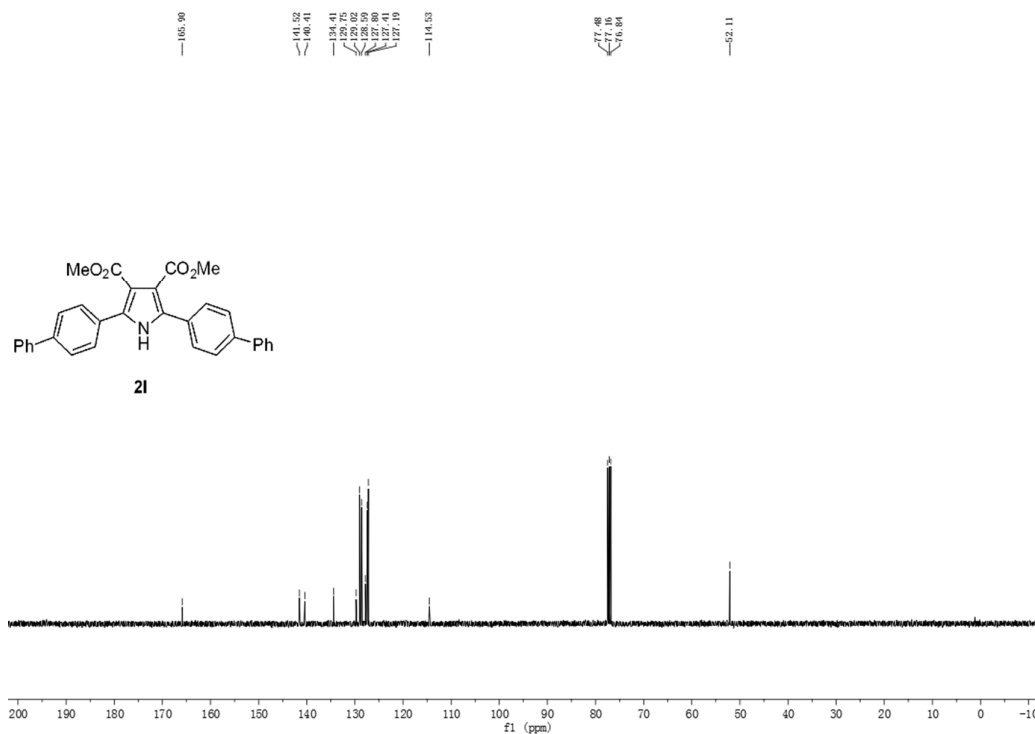
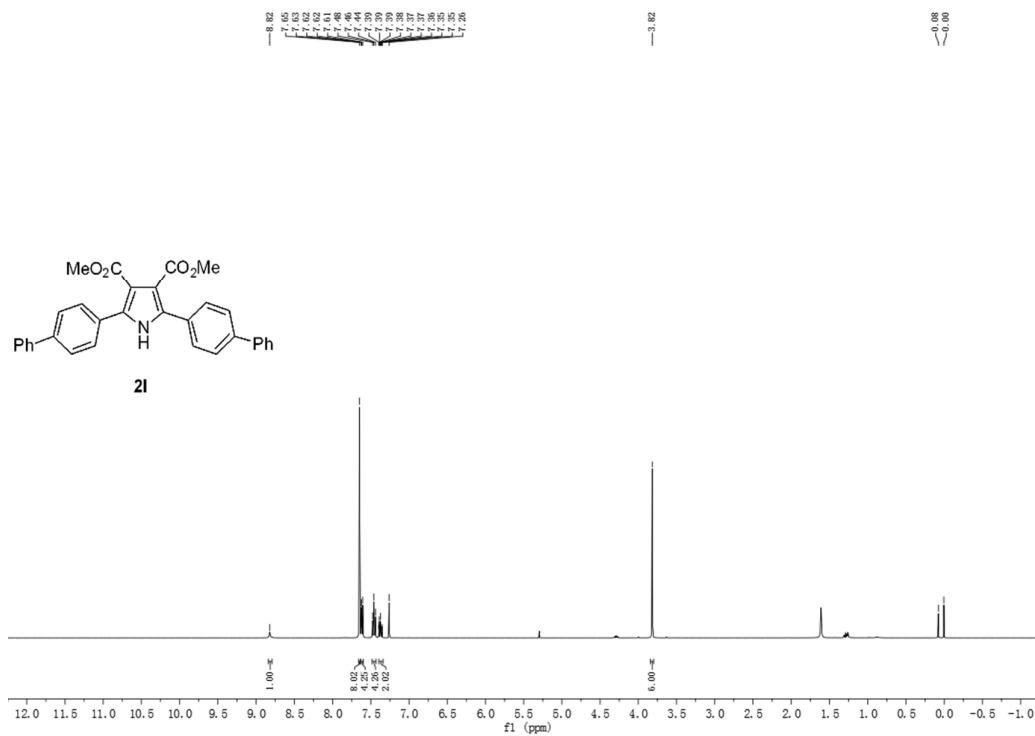


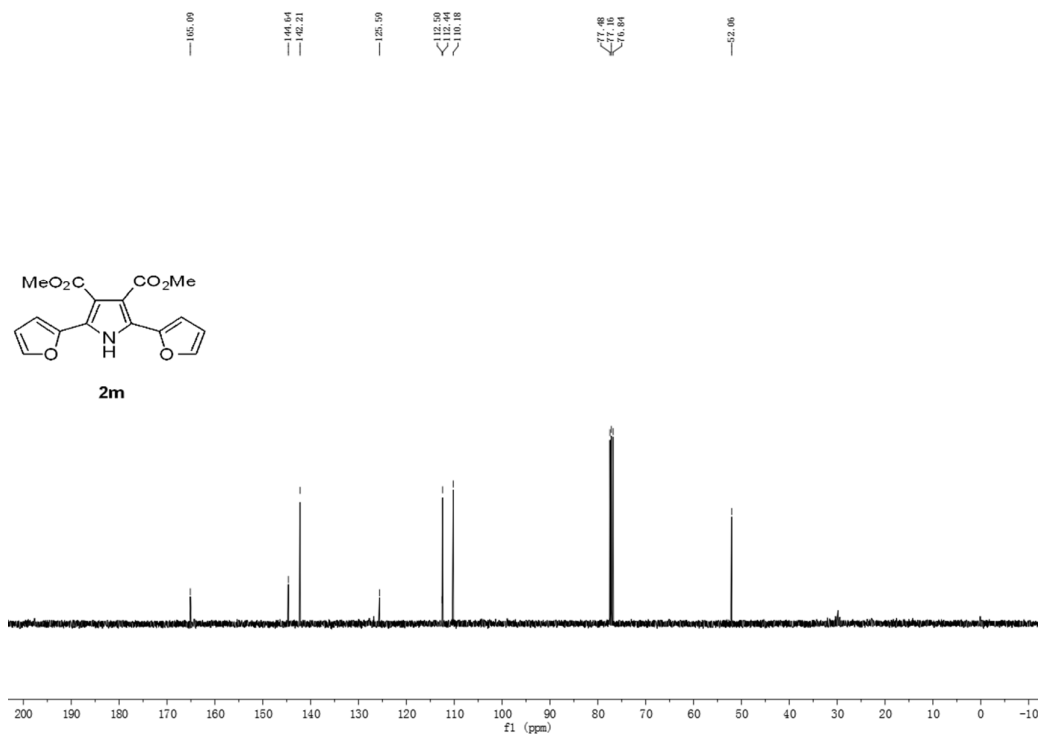
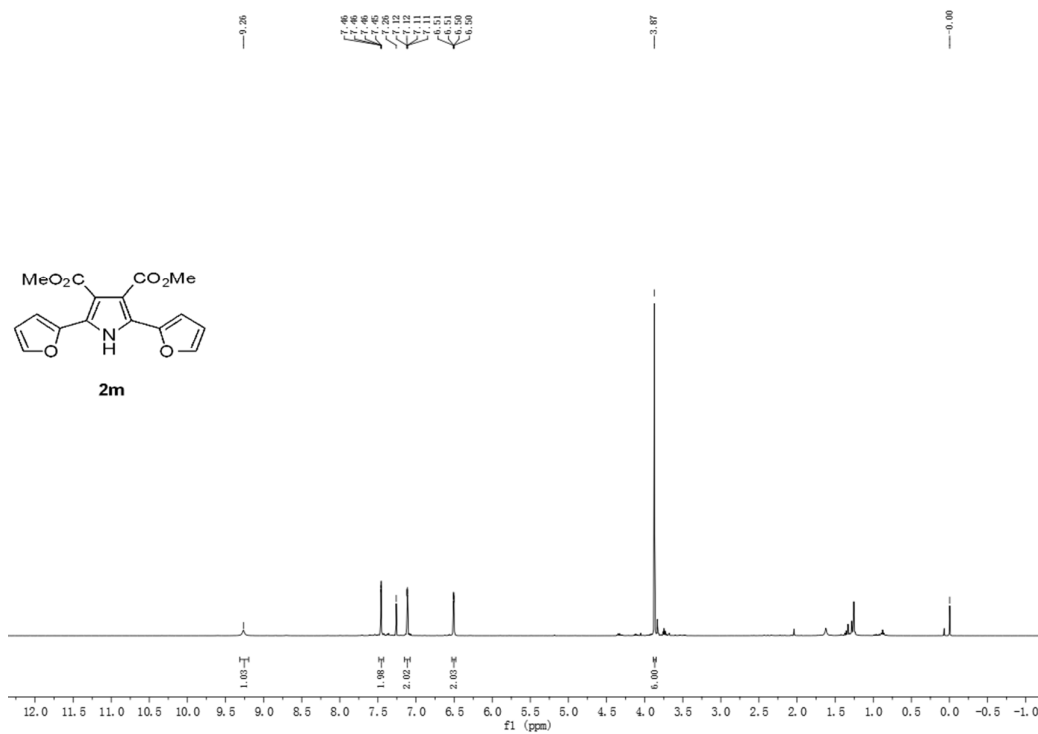


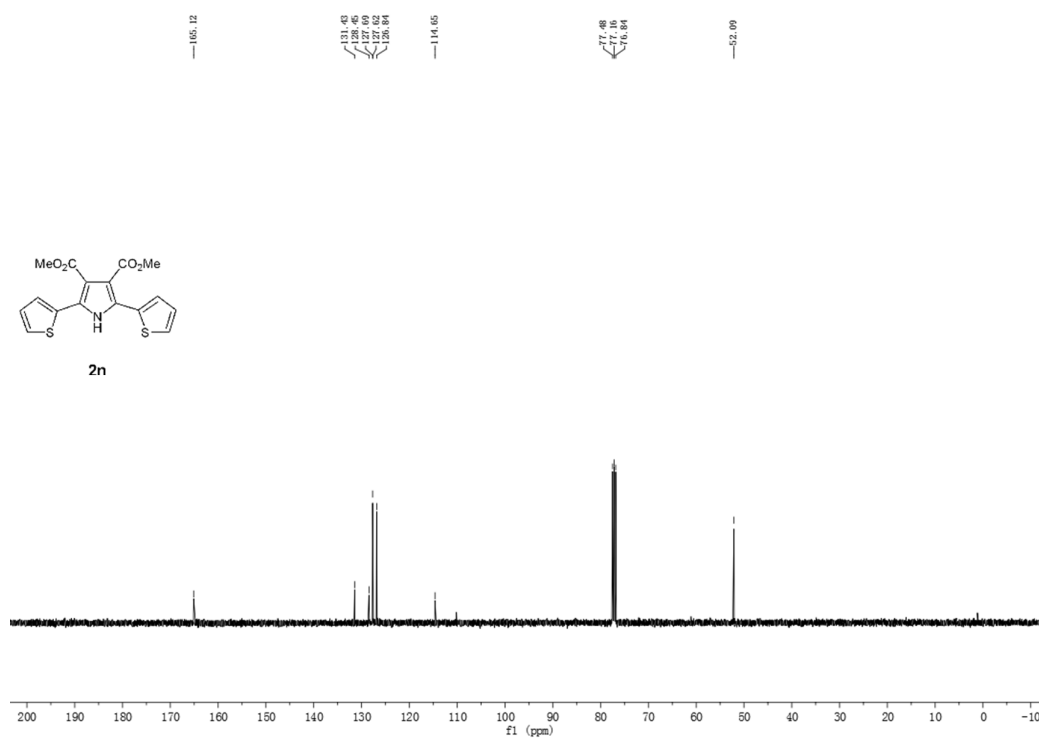
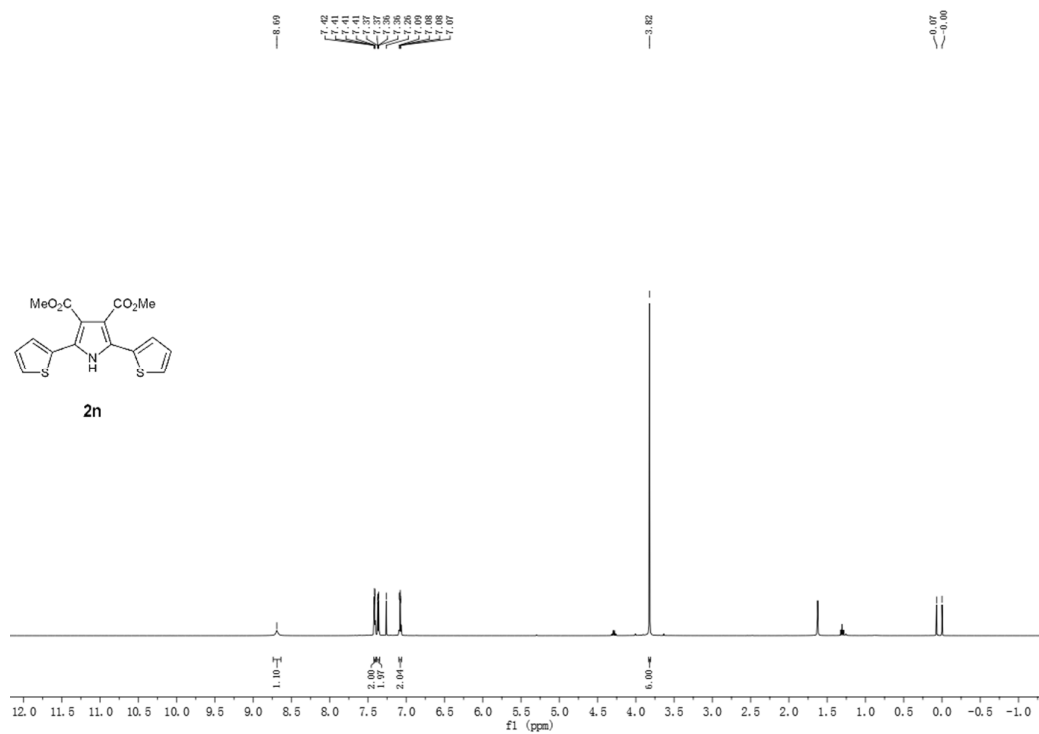


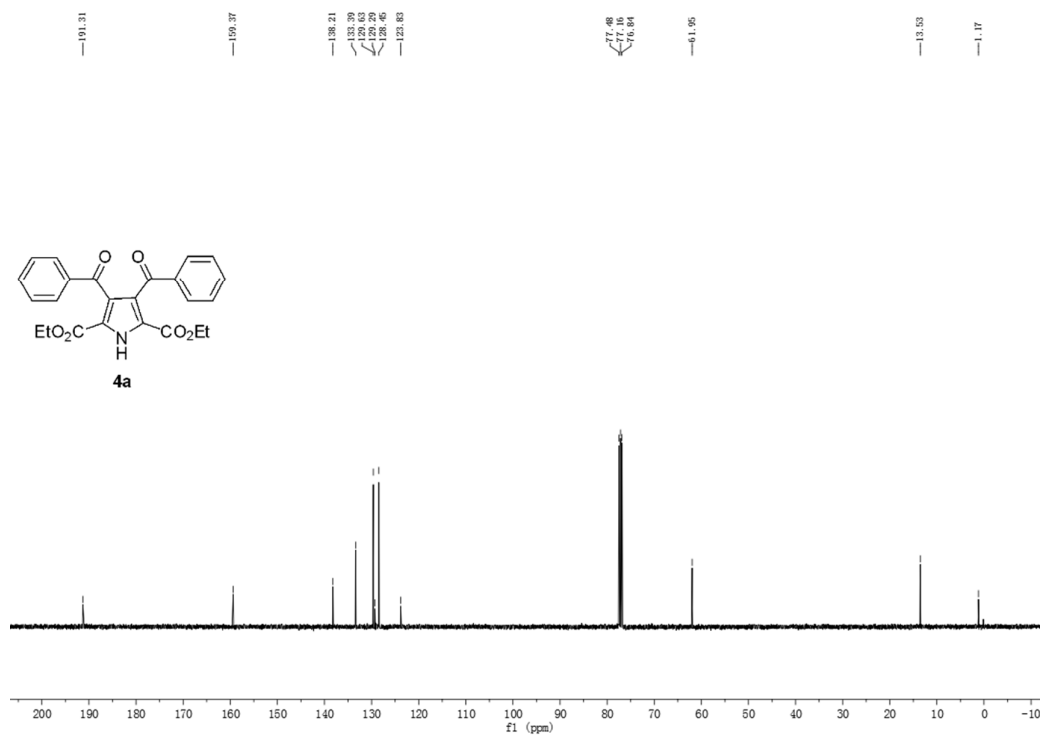
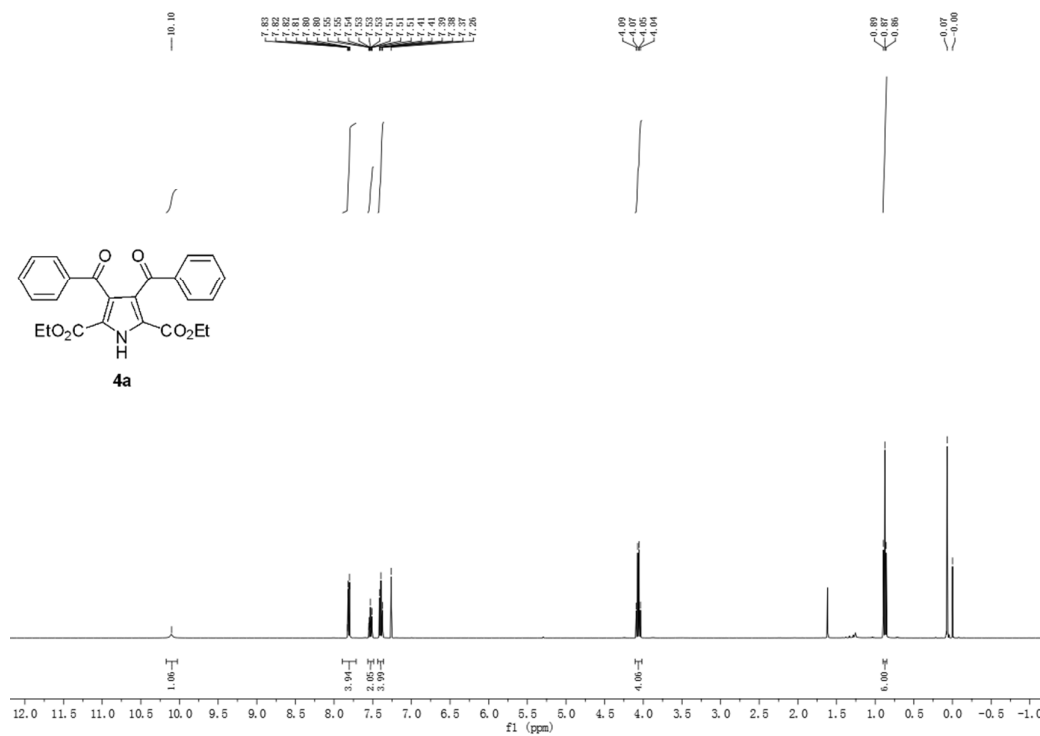


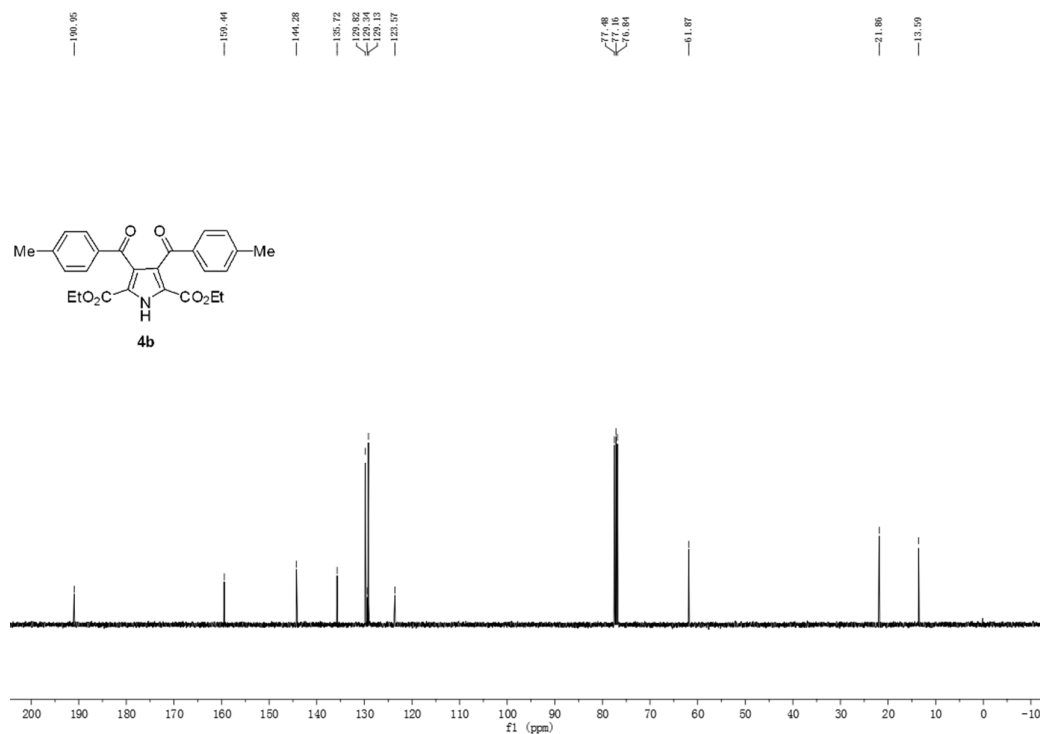
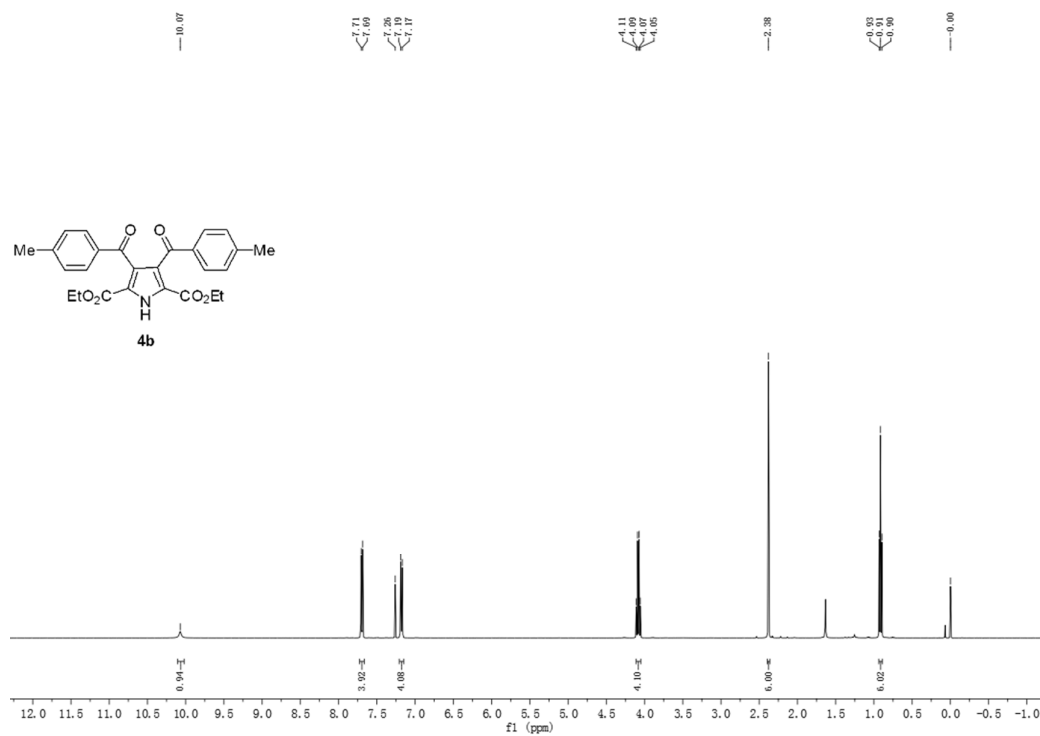


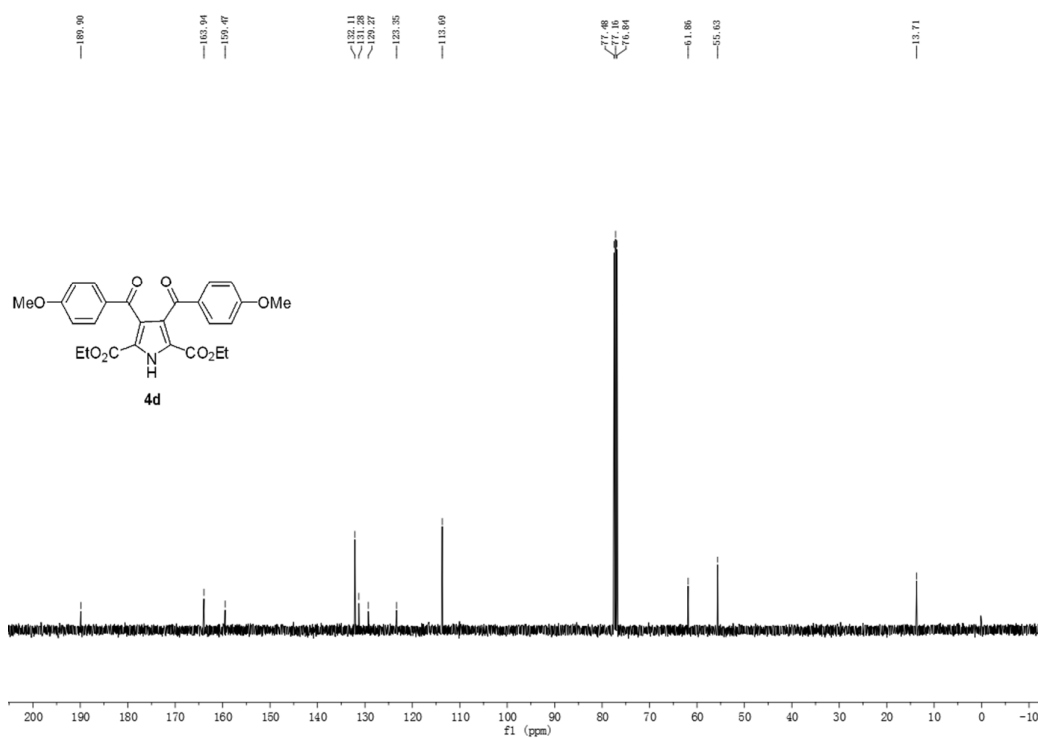
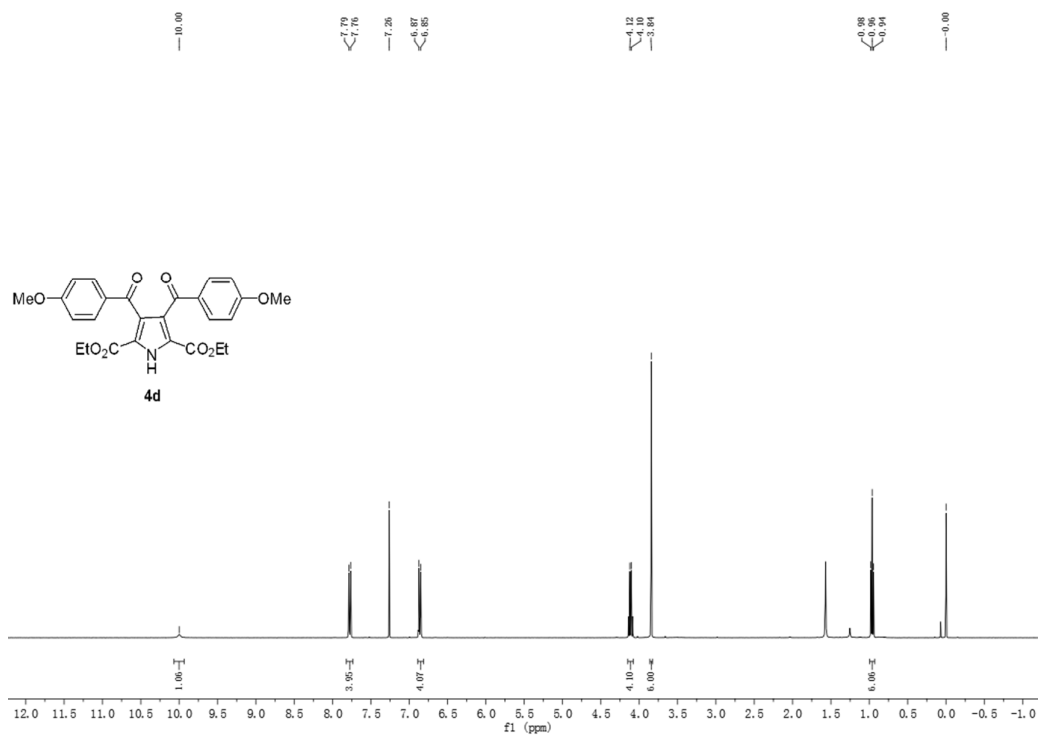


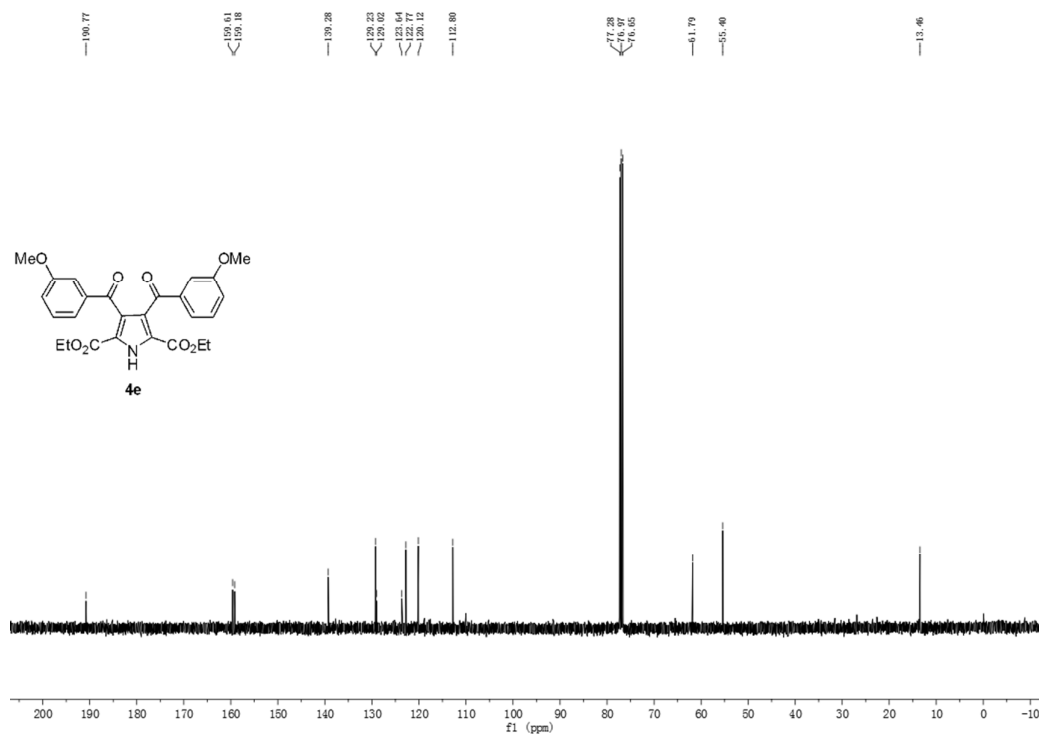
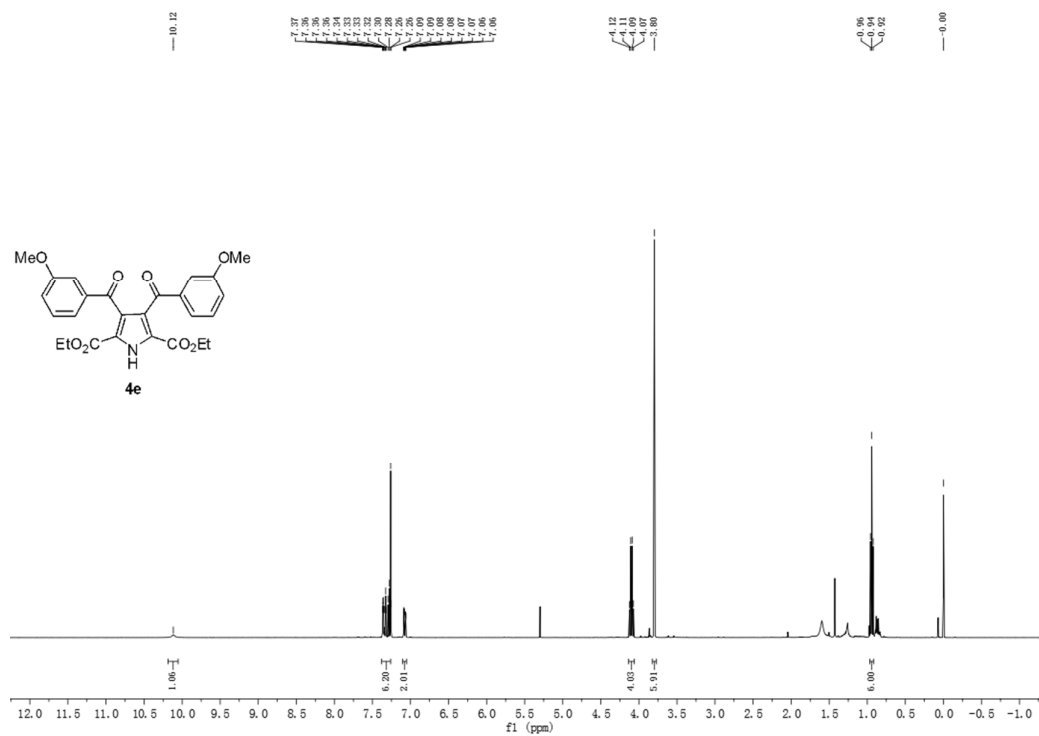


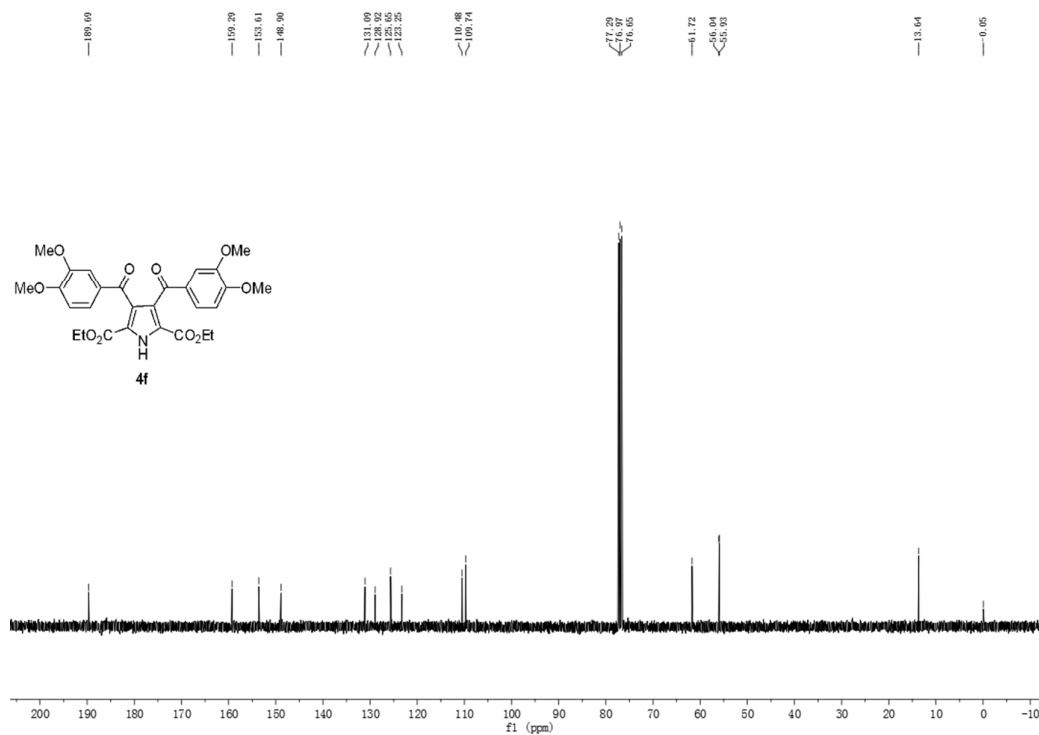
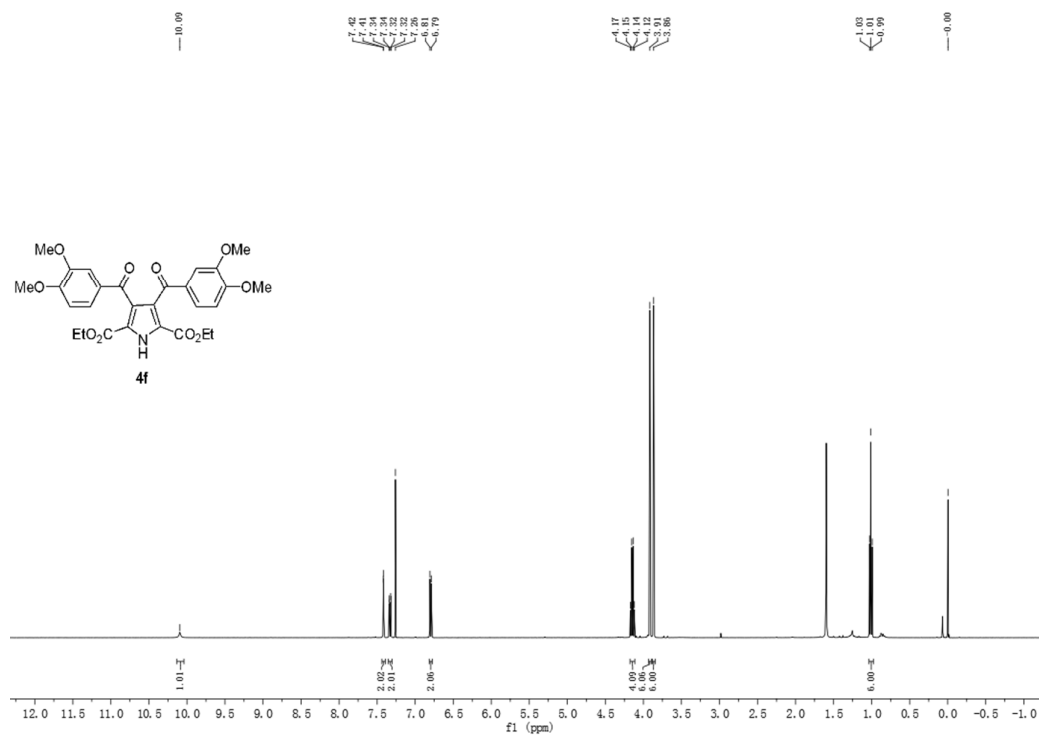


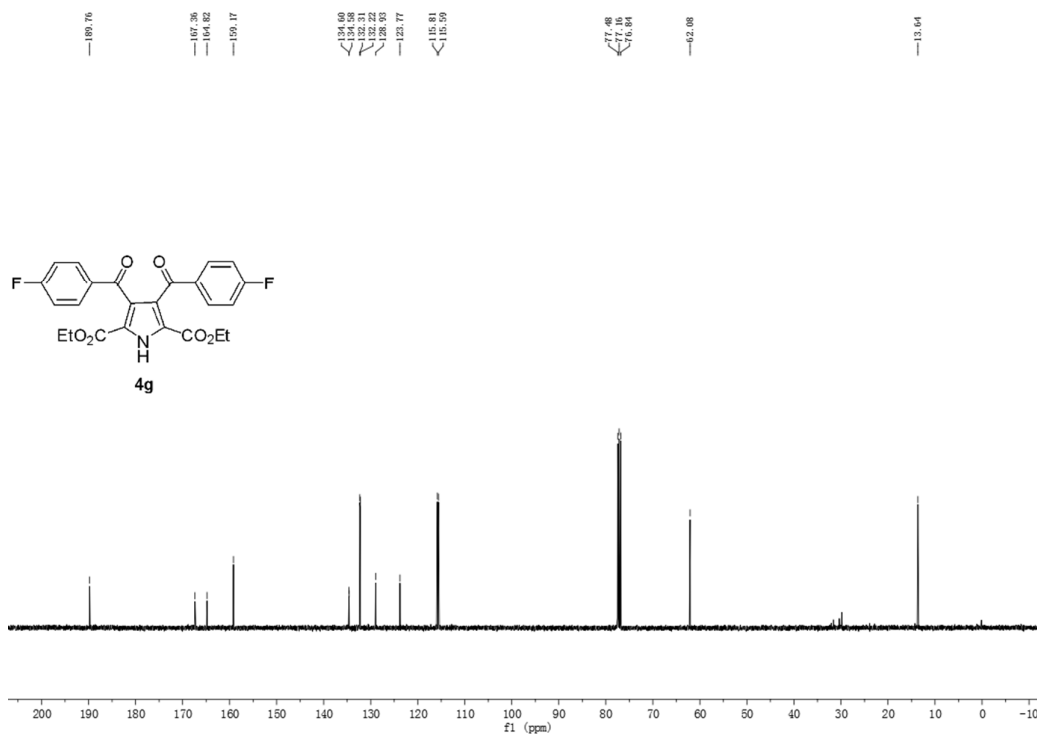
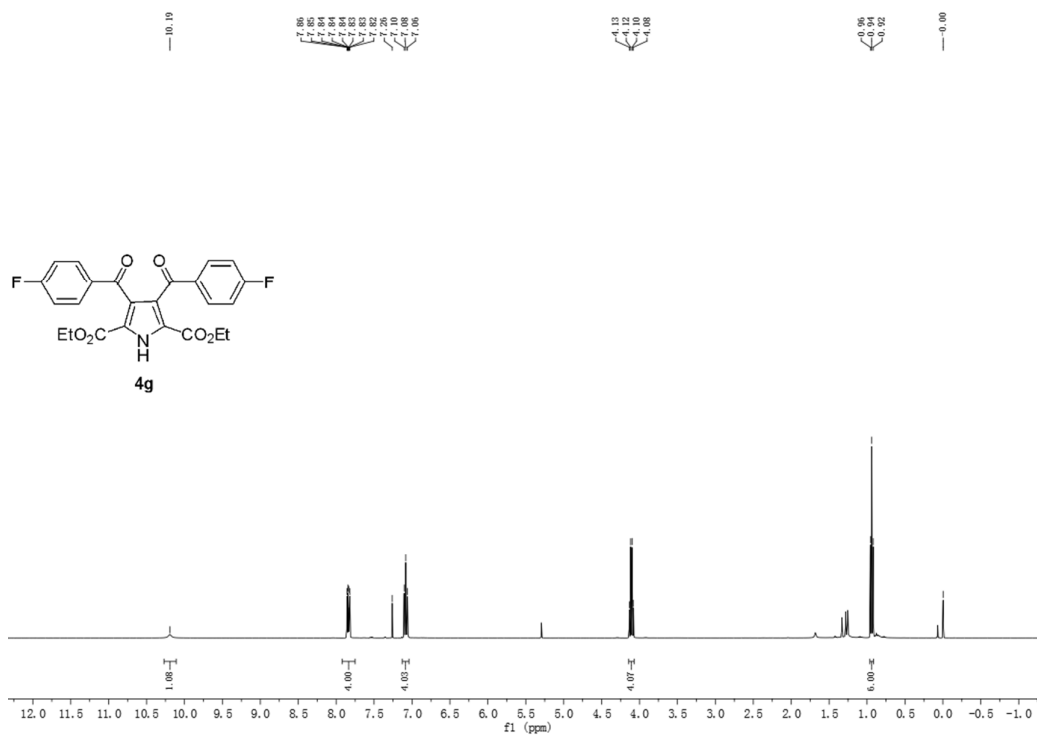


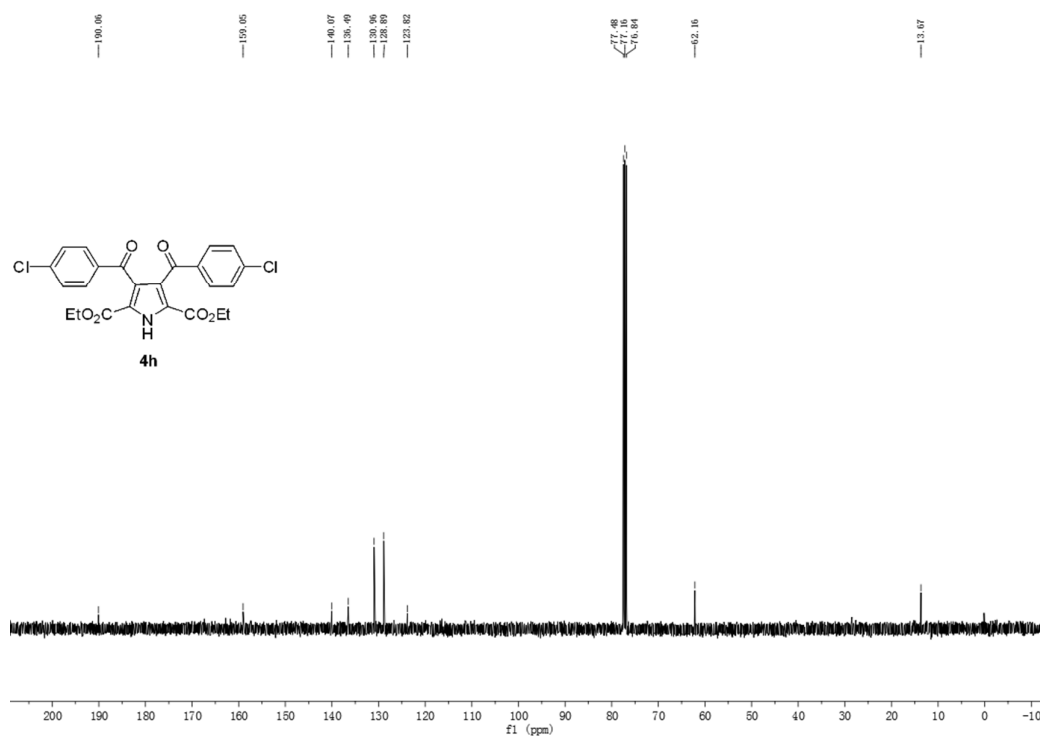
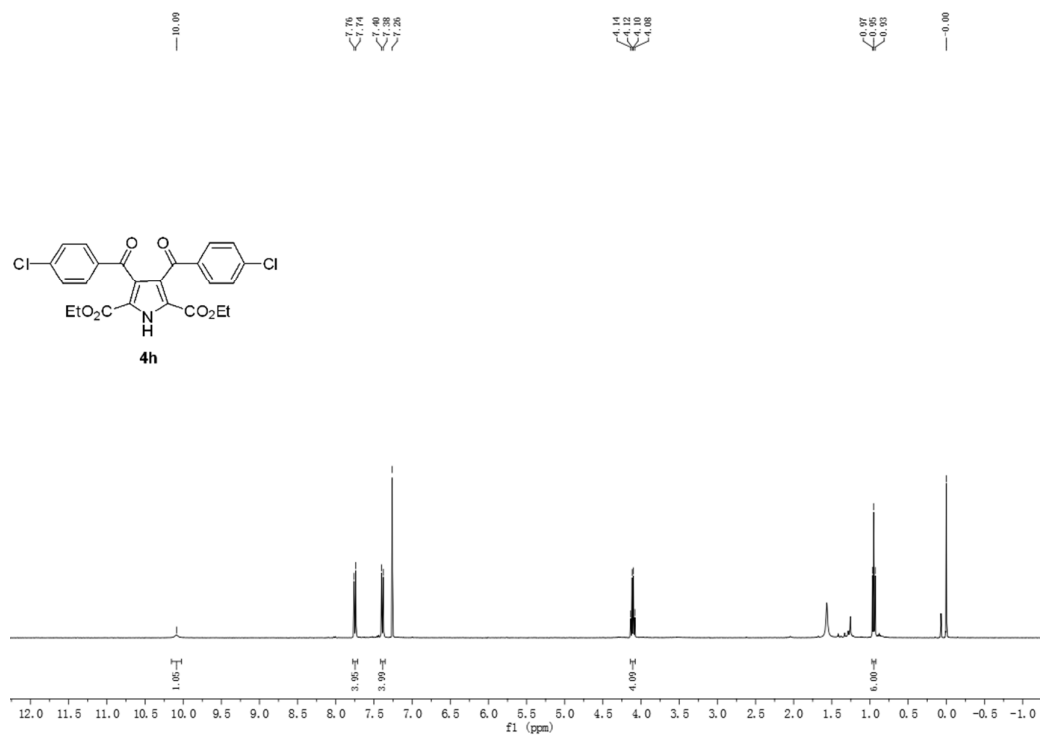


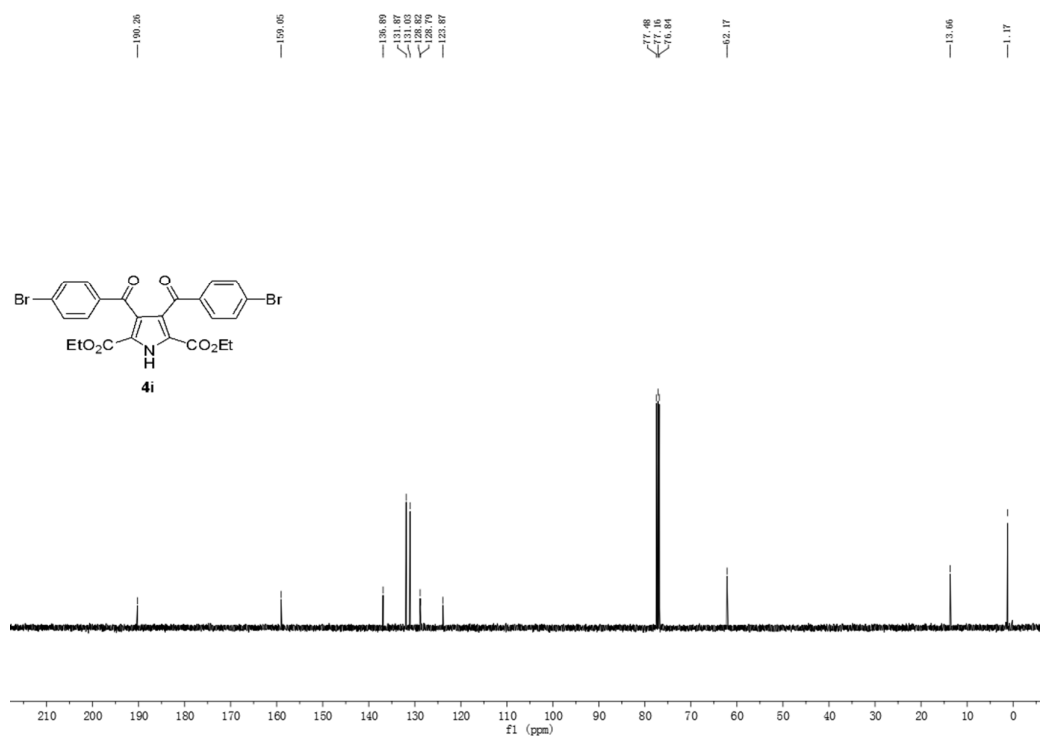
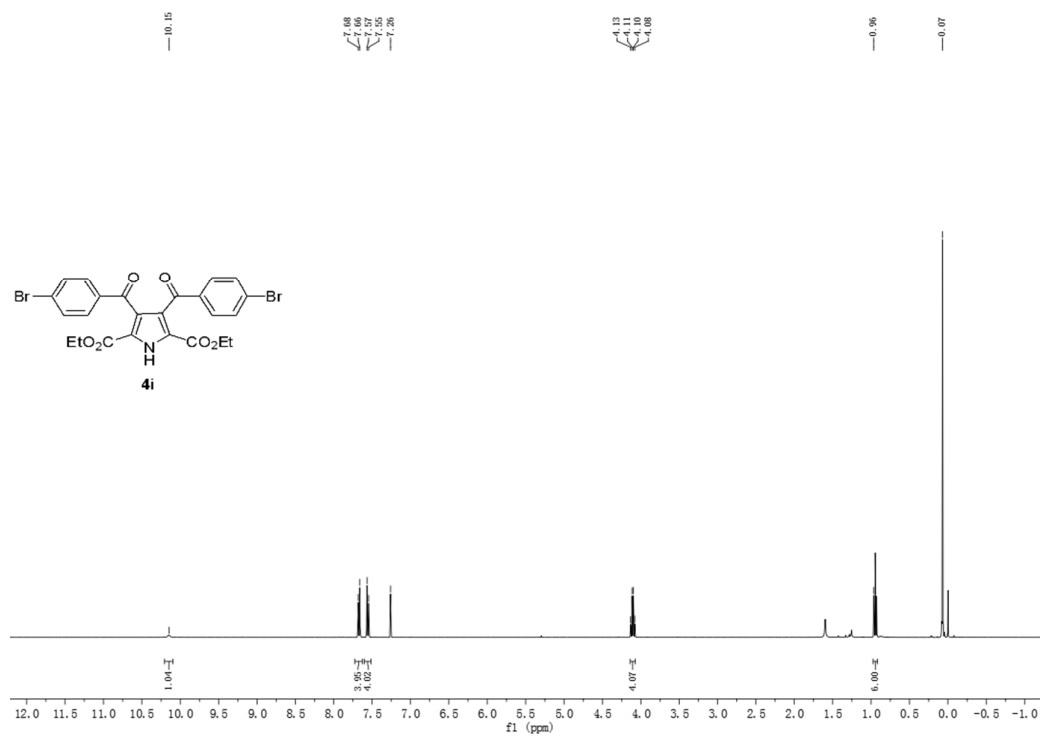


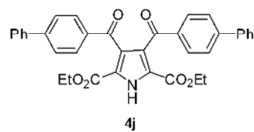
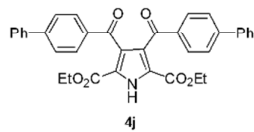


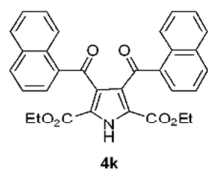
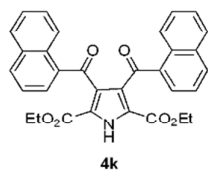


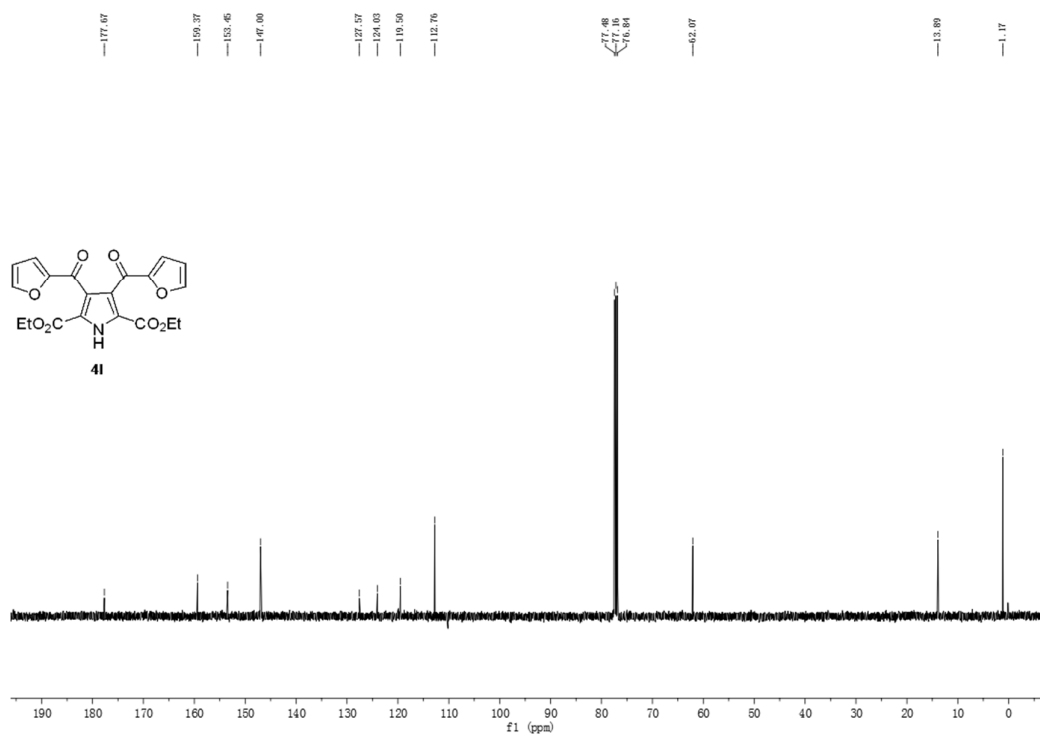
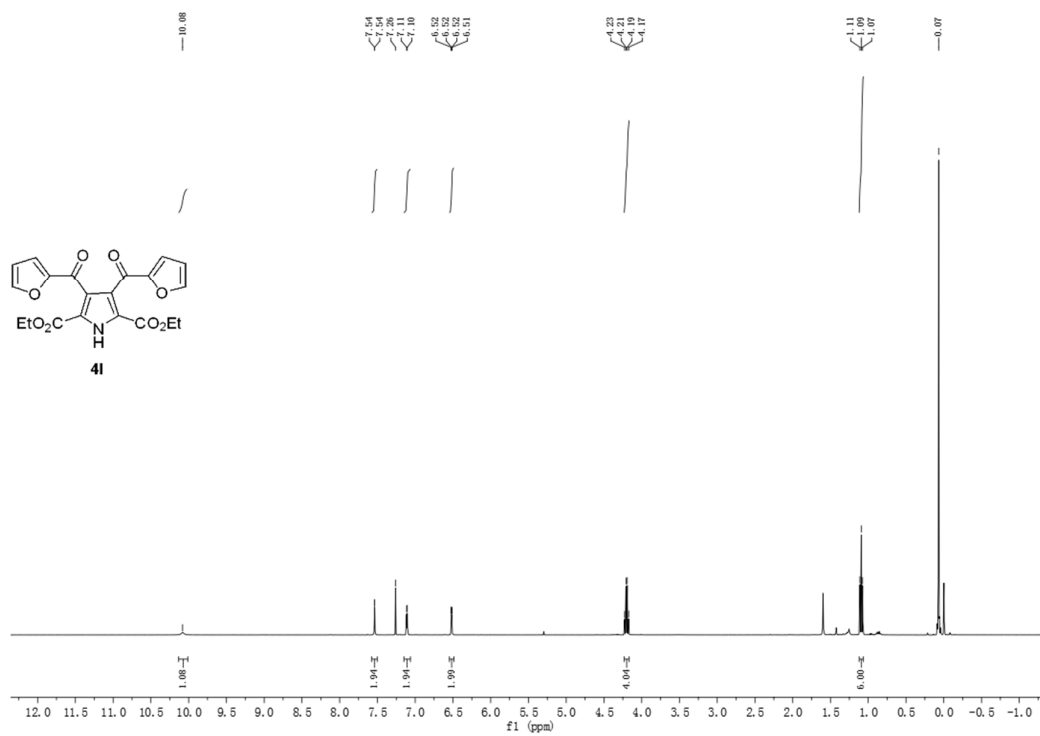


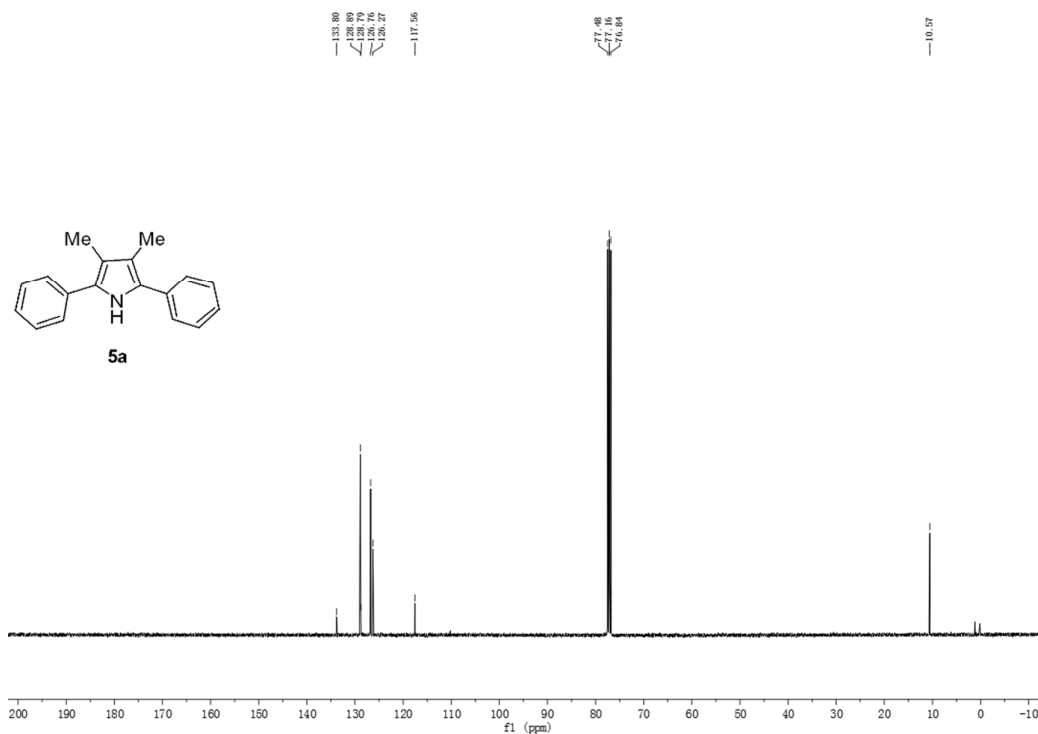
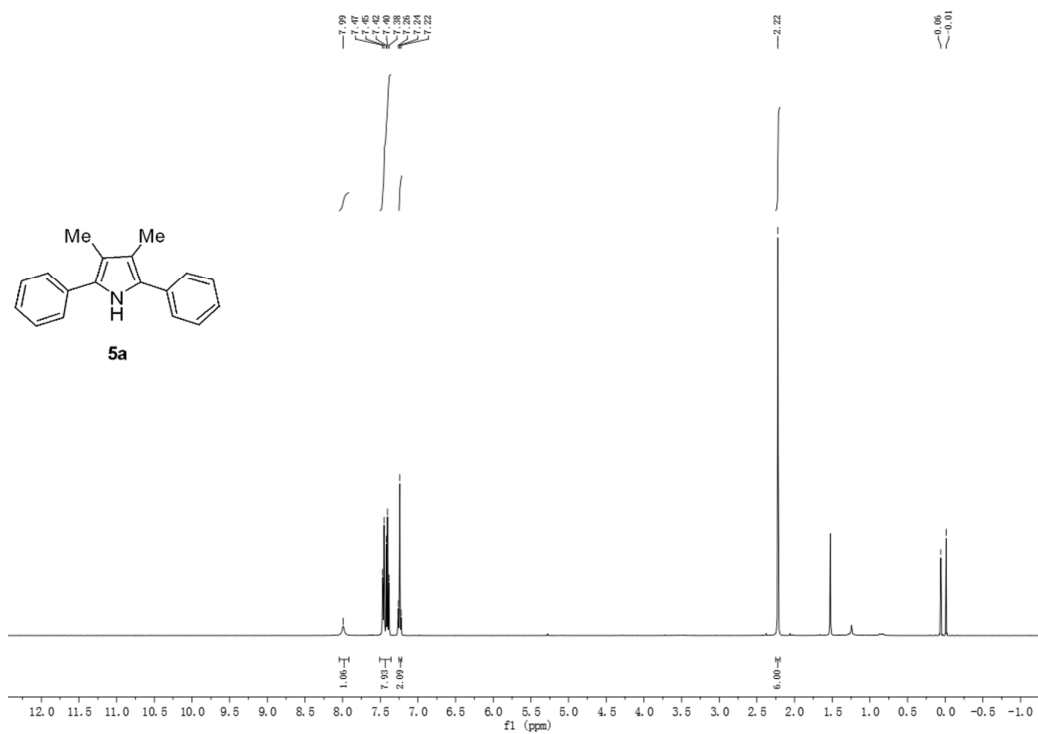


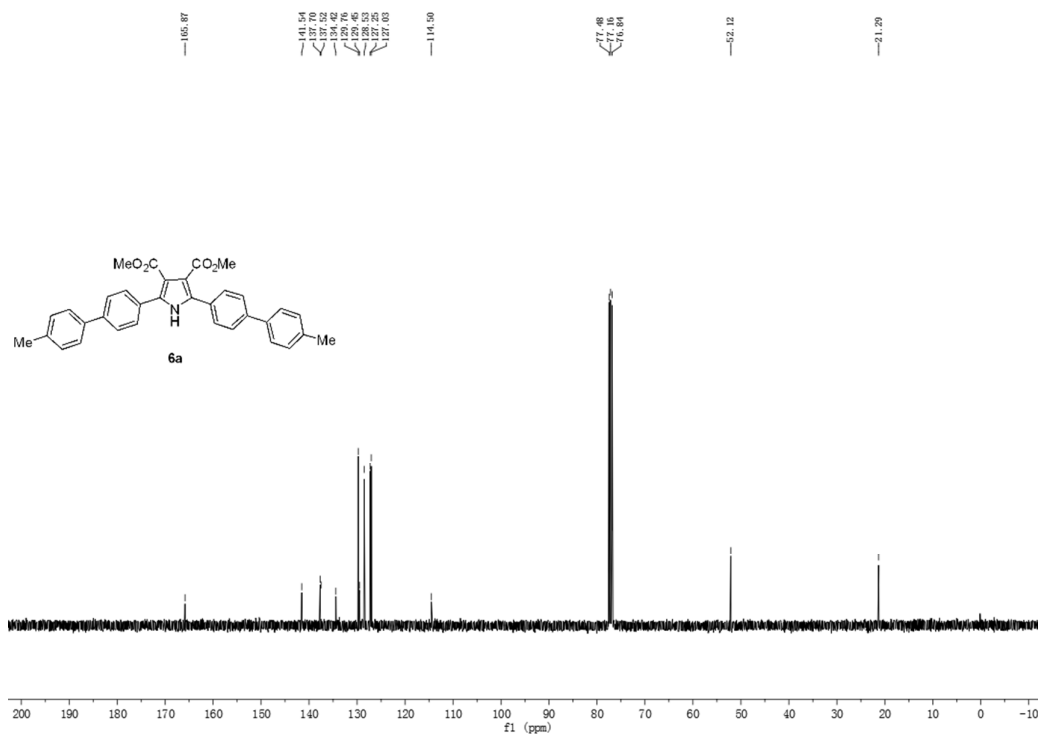
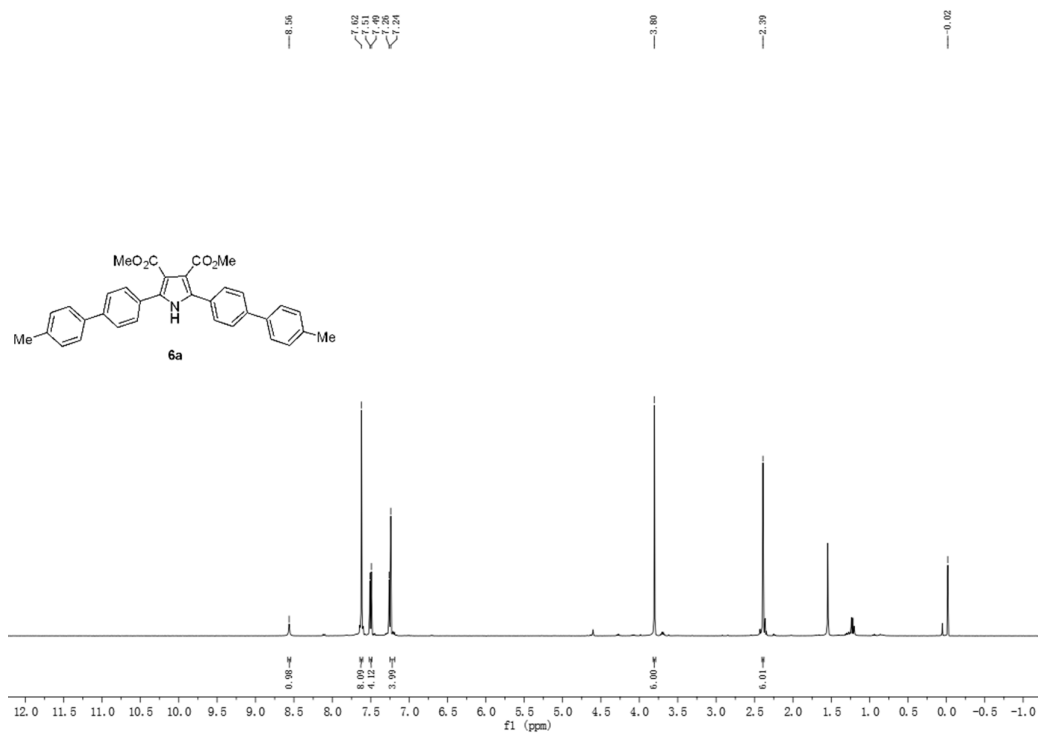






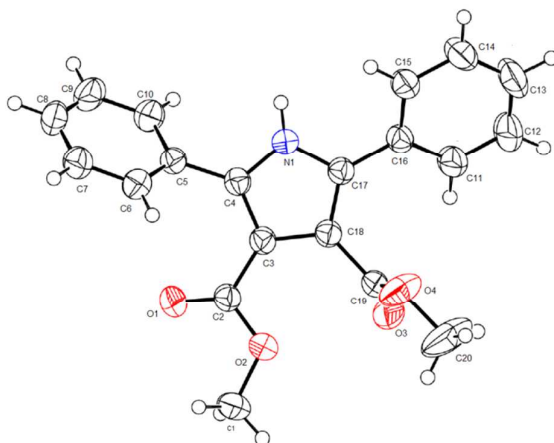






5. X-ray structure report of 2a and 4a

X-ray structure report of 2a



Bond precision: C-C = 0.0021 Å Wavelength=0.71073

Cell: a=13.9835(19) b=9.8343(13) c=13.1233(17)

alpha=90 beta=100.670(2) gamma=90

Temperature: 296 K

Calculated Reported

Volume 1773.5(4) 1773.5(4)

Space group P 21/c P2(1)/c

Hall group -P 2ybc ?

Moiety formula C₂₀ H₁₇ N O₄ ?

Sum formula C₂₀ H₁₇ N O₄ C₂₀ H₁₇ N O₄

Mr 335.35 335.35

D_x, g cm⁻³ 1.256 1.256

Z 4 4

Mu (mm⁻¹) 0.088 0.088

F₀₀₀ 704.0 704.0

F₀₀₀' 704.36

h,k,l_{max} 16,11,15 16,11,15

N_{ref} 3166 3162

T_{min}, T_{max} 0.968, 0.978 0.969, 0.978

T_{min}' 0.968

Correction method= # Reported T Limits: T_{min}=0.969 T_{max}=0.978

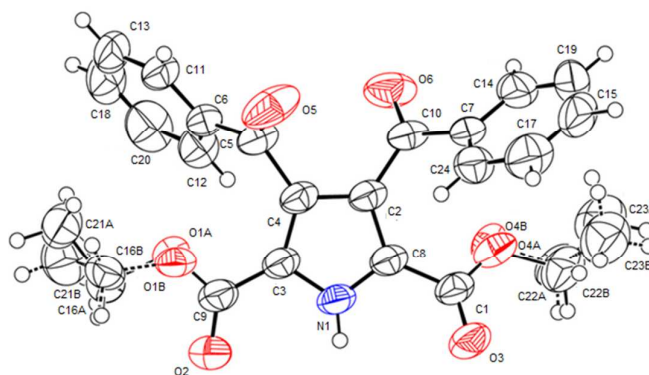
AbsCorr = NONE

Data completeness= 0.999 Theta(max)= 25.100

R(reflections)= 0.0379(2765) wR₂(reflections)= 0.1086(3162)

S = 1.062 N_{par}= 229

X-ray structure report of 4a



Bond precision: C-C = 0.0035 Å Wavelength=0.71073

Cell: a=7.3578(5) b=12.184(1) c=13.0111(10)

alpha=86.190(2) beta=75.871(2) gamma=74.332(2)

Temperature: 299 K

Calculated Reported

Volume 1089.10(14) 1089.10(14)

Space group P -1 P-1

Hall group -P 1 ?

Moiety formula C₂₄ H₂₁ N O₆ ?

Sum formula C₂₄ H₂₁ N O₆ C₂₄ H₂₁ N O₆

Mr 419.42 419.42

D_x,g cm⁻³ 1.279 1.279

Z 2 2

Mu (mm⁻¹) 0.092 0.092

F₀₀₀ 440.0 440.0

F₀₀₀' 440.24

h,k,l_{max} 9,15,16 9,15,16

N_{ref} 4267 4239

T_{min},T_{max} 0.984,0.991 0.982,0.991

T_{min}' 0.982

Correction method= # Reported T Limits: T_{min}=0.982 T_{max}=0.991

AbsCorr = MULTI-SCAN

Data completeness= 0.993 Theta(max)= 26.000

R(reflections)= 0.0560(3368) wR₂(reflections)= 0.1936(4239)

S = 1.145 N_{par}= 340
