

Catalytic asymmetric Michael/cyclization of 3-isothiocyanato thiobutyrolactone: an approach to the construction of a library of bispairo[pyrazolone-thiobutyrolactone] skeletons

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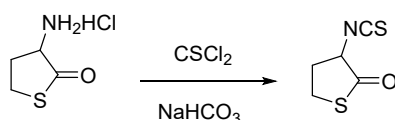
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1. General information

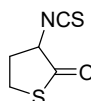
Reactions were monitored by thin layer chromatography using UV light to visualize the course of reaction. Purification of reaction products was carried out by flash chromatography on silica gel or just by simple filtration and washing. ^1H and ^{13}C NMR spectra were obtained using a Bruker DPX-400 spectrometer. ^1H NMR chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR chemical shifts are reported in ppm (δ) from tetramethylsilane (TMS) with the solvent resonance as the internal standard. Melting points were measured on an electrothermal digital melting point apparatus.

2. General procedure for preparation of 3-isothiocyanato thiobutyrolactone 1



The homocysteinethiolactone hydrochloride (1.53 g, 10.0 mmol) was dissolved in CH₂Cl₂ (90 mL), and saturated aqueous NaHCO₃ (90 mL) was added at 0 °C. The biphasic mixture was stirred vigorously for 15 min. The stirring was stopped, and thiophosgene (1.71 g, 1.14 mL, 15.0 mmol) was added via syringe to the organic layer. Stirring was immediately restarted, and the reaction was allowed to stir for 2 h at 0 °C. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (2×50 mL) and washed with water (50 mL). The combined organics were dried over Na₂SO₄, concentrated under vacuum. The residue mixture was purified by flash column chromatography on silica gel to give 3-isothiocyanato thiobutyrolactone 1.

3. Characterization data of compound 1

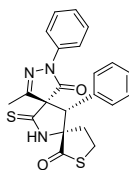


1: Light yellow oil; yield 73%, 1.16 g; ^1H NMR (CDCl₃, 400 MHz) δ : 2.25-2.35 (m, 1H), 2.65-2.72 (m, 1H), 3.34-3.38 (m, 2H), 4.43-4.47 (m, 1H); ^{13}C NMR (CDCl₃, 100 MHz) δ : 27.5, 31.9, 64.0, 199.8; HRMS (ESI-TOF) m/z : Calcd. for C₅H₅NNaOS₂ [M+Na]⁺: 181.9705; Found: 181.9703.

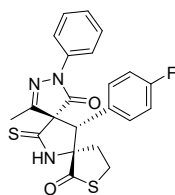
4. Catalytic asymmetric synthesis of bispiro[pyrazolone-thiobutyrolactone] skeletons 3

In a sealed tube equipped with a magnetic stirring bar, to the mixture of 3-isothiocyanato thiobutyrolactone **1** (0.10 mmol), and squaramide catalyst **C12** (10 mol %) in 1.5 mL of freshly distilled toluene was added alkylidene pyrazolone **2** (0.15 mmol). The reaction mixture was stirred at room temperature for 16 h and was directly loaded onto a silica gel and purified by flash chromatography to give the desired product **3**, using hexane/EtOAc (10/1, v/v) as the eluent.

5. Characterization data of compounds 3

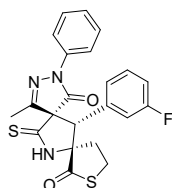


3a: Light yellow solid, m.p. 207.9-208.5 °C; yield 87%, 36.6 mg, 93% ee, >20:1 dr, $[\alpha]_D^{20} = +151.3$ (*c* 2.1, CHCl₃); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{major} = 11.61$ min; $\tau_{minor} = 7.15$ min); ¹H NMR (CDCl₃, 400 MHz) δ : 2.18 (s, 3H), 2.57-2.65 (m, 1H), 2.72-2.78 (m, 1H), 3.12-3.26 (m, 2H), 4.39 (s, 1H), 7.12-7.16 (m, 1H), 7.19-7.23 (m, 3H), 7.27-7.34 (m, 4H), 7.75 (d, *J* = 8.0 Hz, 2H), 9.50 (br s, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ : 11.8, 25.3, 32.5, 51.0, 75.0, 76.7, 117.1, 123.5, 126.6, 127.0, 127.5, 128.1, 135.1, 155.6, 167.1, 193.3, 201.5; HRMS (ESI-TOF) *m/z*: Calcd. for C₂₂H₁₉N₃NaO₂S₂ [M+Na]⁺: 444.0811; Found: 444.0813.

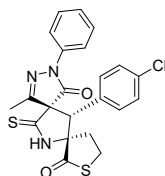


3b: Light yellow solid, m.p. 134.2-134.7 °C; yield 85%, 37.3 mg, 91% ee, >20:1 dr, $[\alpha]_D^{20} = +163.0$ (*c* 2.9, CHCl₃); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{major} = 11.04$ min; $\tau_{minor} = 6.30$ min); ¹H NMR (CDCl₃, 400 MHz) δ : 2.21 (s, 3H), 2.71-2.79 (m, 2H), 2.89-2.95 (m, 1H), 3.41-3.45 (m, 1H), 4.33 (s, 1H), 7.18-7.27 (m, 3H), 7.42-7.51 (m, 4H), 7.71 (d, *J* = 8.4 Hz, 2H), 11.86 (br s, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ : 14.2, 27.6, 35.0, 52.5, 77.4, 79.2, 116.6 (d, *J*_{CF} = 22.3 Hz), 119.2, 126.3, 127.2, 127.3, 129.6, 132.4 (d, *J*_{CF} = 9.2 Hz), 137.3, 159.2, 163.7 (d, *J*_{CF} = 245.1 Hz), 169.4,

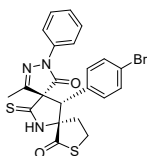
194.2, 205.7; ^{19}F NMR (CDCl_3 , 470 MHz) δ : -111.41; HRMS (ESI-TOF) m/z : Calcd. for $\text{C}_{22}\text{H}_{18}\text{FN}_3\text{NaO}_2\text{S}_2$ $[\text{M}+\text{Na}]^+$: 462.0717; Found: 462.0714.



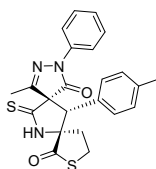
3c: Light yellow solid, m.p. 163.2-164.0 °C; yield 84%, 36.9 mg, 98% ee, >20:1 dr, $[\alpha]_{\text{D}}^{20} = +119.4$ (c 2.9, CHCl_3); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{\text{major}} = 8.61$ min; $\tau_{\text{minor}} = 5.68$ min); ^1H NMR ($\text{DMSO-}d_6$, 400 MHz) δ : 2.22 (s, 3H), 2.70-2.82 (m, 2H), 2.90-2.95 (m, 1H), 3.41-3.47 (m, 1H), 4.35 (s, 1H), 7.19-7.30 (m, 4 H), 7.39-7.47 (m, 3H), 7.71 (d, $J = 7.6$ Hz, 2H), 11.89 (br s, 1H); ^{13}C NMR ($\text{DMSO-}d_6$, 100 MHz) δ : 14.2, 27.7, 35.1, 52.6, 77.3, 79.2, 116.8 (d, $J_{\text{CF}} = 21.4$ Hz), 117.1 (d, $J_{\text{CF}} = 23.1$ Hz), 119.1, 126.3, 126.4, 129.7, 131.7 (d, $J_{\text{CF}} = 9.2$ Hz), 133.6 (d, $J_{\text{CF}} = 8.3$ Hz), 137.3, 159.2, 162.6 (d, $J_{\text{CF}} = 244.4$ Hz), 170.0, 194.0, 205.5; ^{19}F NMR (CDCl_3 , 470 MHz) δ : -111.41; HRMS (ESI-TOF) m/z : Calcd. for $\text{C}_{22}\text{H}_{18}\text{FN}_3\text{NaO}_2\text{S}_2$ $[\text{M}+\text{Na}]^+$: 462.0717; Found: 462.0717.



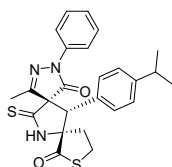
3d: Light yellow solid, m.p. 184.5-185.6 °C; yield 85%, 38.7 mg, 99% ee, >20:1 dr, $[\alpha]_{\text{D}}^{20} = +206.7$ (c 2.9, CHCl_3); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{\text{major}} = 11.36$ min; $\tau_{\text{minor}} = 6.05$ min); ^1H NMR ($\text{DMSO-}d_6$, 400 MHz) δ : 2.21 (s, 3H), 2.70-2.82 (m, 2H), 2.89-2.95 (m, 1H), 3.41-3.47 (m, 1H), 4.32 (s, 1H), 7.23-7.27 (m, 1H), 7.42-7.47 (m, 6H), 7.70-7.73 (m, 2H), 11.88 (br s, 1H); ^{13}C NMR ($\text{DMSO-}d_6$, 100 MHz) δ : 14.2, 27.7, 35.0, 52.5, 77.3, 79.2, 119.3, 126.3, 129.6, 129.7, 130.0, 132.1, 134.7, 137.3, 159.1, 169.6, 194.1, 205.6; HRMS (ESI-TOF) m/z : Calcd. for $\text{C}_{22}\text{H}_{18}\text{ClN}_3\text{NaO}_2\text{S}_2$ $[\text{M}+\text{Na}]^+$: 478.0421; Found: 478.0424.



3e: Light yellow solid, m.p. 130.2-130.8 °C; yield 86%, 42.9 mg, >99% ee, >20:1 dr, $[\alpha]_D^{20} = +146.1$ (*c* 2.9, CHCl₃); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{major} = 12.13$ min; $\tau_{minor} = 6.16$ min); ¹H NMR (CDCl₃, 400 MHz) δ : 2.21 (s, 3H), 2.69-2.82 (m, 2H), 2.89-2.95 (m, 1H), 3.40-3.46 (m, 1H), 4.30 (s, 1H), 7.23-7.27 (m, 1H), 7.38-7.46 (m, 4H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 2H), 11.88 (br s, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ : 14.2, 27.7, 35.0, 52.6, 77.2, 79.1, 119.3, 123.4, 126.3, 129.6, 130.4, 132.4, 132.6, 137.3, 159.1, 169.6, 194.1, 205.6; HRMS (ESI-TOF) *m/z*: Calcd. for C₂₂H₁₈BrN₃NaO₂S₂ [M+Na]⁺: 521.9916; Found: 521.9914.

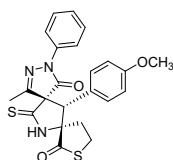


3f: Light yellow solid, m.p. 179.2-179.9 °C; yield 82%, 35.7 mg, 93% ee, >20:1 dr, $[\alpha]_D^{20} = +229.6$ (*c* 2.5, CHCl₃); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{major} = 13.71$ min; $\tau_{minor} = 7.51$ min); ¹H NMR (DMSO-*d*₆, 400 MHz) δ : 2.19 (s, 3H), 2.20 (s, 3H), 2.69-2.82 (m, 2H), 2.89-2.93 (m, 1H), 3.38-3.40 (m, 1H), 4.26 (s, 1H), 7.11-7.14 (m, 2H), 7.21-7.25 (m, 1H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.41-7.45 (m, 2H), 7.74-7.76 (m, 2H), 11.83 (br s, 1H); ¹³C NMR (DMSO-*d*₆, 100 MHz) δ : 14.2, 21.0, 27.6, 35.1, 53.4, 77.4, 79.2, 119.0, 126.1, 127.9, 129.6, 130.0, 130.2, 137.4, 139.3, 159.1, 169.8, 194.4, 206.0; HRMS (ESI-TOF) *m/z*: Calcd. for C₂₃H₂₁N₃NaO₂S₂ [M+Na]⁺: 458.0967; Found: 458.0962.

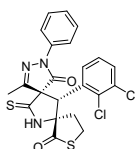


3g: Light yellow solid, m.p. 184.2-185.1 °C; yield 90%, 41.7 mg, 93% ee, >20:1 dr, $[\alpha]_D^{20} = +289.1$ (*c* 2.2, CHCl₃); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{major} = 10.45$ min; $\tau_{minor} = 6.73$ min);

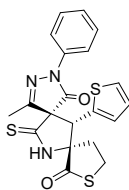
¹H NMR (DMSO-*d*₆, 400 MHz) δ : 1.09-1.11 (m, 6H), 2.19 (s, 3H), 2.67-2.83 (m, 3H), 2.90-2.94 (m, 1H), 4.30 (s, 1H), 7.19-7.31 (m, 5H), 7.42-7.46 (m, 2H), 7.74 (d, *J* = 7.6 Hz, 2H), 11.84 (br s, 1H); ¹³C NMR (DMSO-*d*₆, 100 MHz) δ : 14.2, 23.9, 24.1, 27.6, 33.4, 35.2, 53.2, 77.3, 79.2, 119.1, 126.1, 127.6, 128.4, 129.6, 130.0, 137.5, 149.8, 159.2, 169.8, 194.4, 205.9; HRMS (ESI-TOF) *m/z*: Calcd. for C₂₅H₂₅N₃NaO₂S₂ [M+Na]⁺: 486.1280; Found: 486.1277.



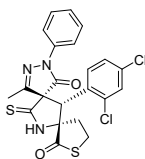
3h: Light yellow solid, m.p. 201.3-201.7 °C; yield 82%, 37.0 mg, 96% ee, 12:1 dr, [α]_D²⁰ = +377.4 (*c* 2.8, CHCl₃); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 16.70 min; τ_{minor} = 9.21 min); ¹H NMR (CDCl₃, 400 MHz) δ : 2.17 (s, 3H), 2.57-2.65 (m, 1H), 2.71-2.77 (m, 1H), 3.09-3.15 (m, 1H), 3.18-3.24 (m, 1H), 3.65 (s, 3H), 4.33 (s, 1H), 6.70 (d, *J* = 8.8 Hz, 2H), 7.11-7.15 (m, 1H), 7.20 (d, *J* = 8.8 Hz, 2H), 7.30-7.34 (m, 2H), 7.75-7.77 (m, 2H), 9.77 (br s, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ : 13.1, 26.6, 33.8, 51.8, 54.2, 75.6, 78.0, 113.6, 118.4, 121.1, 124.8, 127.9, 130.1, 136.4, 157.0, 159.1, 168.4, 194.7, 203.0; HRMS (ESI-TOF) *m/z*: Calcd. for C₂₃H₂₁N₃NaO₃S₂ [M+Na]⁺: 474.0917; Found: 474.0914.



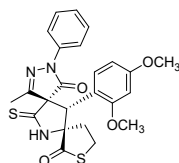
3i: Light yellow solid, m.p. 179.8-179.9 °C; yield 90%, 44.0 mg, 87% ee, >20:1 dr, [α]_D²⁰ = +484.1 (*c* 2.3, CHCl₃); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 23.33 min; τ_{minor} = 8.51 min); ¹H NMR (DMSO-*d*₆, 400 MHz) δ : 2.24 (s, 3H), 2.60-2.67 (m, 1H), 2.80-2.87 (m, 1H), 2.89-2.94 (m, 1H), 3.40-3.43 (m, 1H), 5.17 (s, 1H), 7.22-7.26 (m, 1H), 7.39-7.44 (m, 3H), 7.64-7.69 (m, 3H), 7.87 (d, *J* = 7.2 Hz, 1H), 11.92 (br s, 1H); ¹³C NMR (DMSO-*d*₆, 100 MHz) δ : 14.4, 27.7, 34.7, 47.9, 77.7, 79.0, 119.3, 126.4, 129.0, 129.6, 130.0, 130.8, 132.2, 133.3, 133.4, 137.1, 158.8, 169.3, 193.6, 205.4; HRMS (ESI-TOF) *m/z*: Calcd. for C₂₂H₁₇Cl₂N₃NaO₂S₂ [M+Na]⁺: 512.0031; Found: 512.0027.



3j: Light yellow solid, m.p. 161.5-161.8 °C; yield 84%, 35.9 mg, 96% ee, >20:1 dr, $[\alpha]_{\text{D}}^{20} = +192.2$ (*c* 2.4, CHCl₃); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{\text{major}} = 13.38$ min; $\tau_{\text{minor}} = 7.70$ min); ¹H NMR (DMSO-*d*₆, 400 MHz) δ : 2.19 (s, 3H), 2.58-2.64 (m, 1H), 2.78-2.85 (m, 1H), 2.89-2.94 (m, 1H), 3.38-3.41 (m, 1H), 4.67 (s, 1H), 7.00-7.02 (m, 1H), 7.17 (d, *J* = 3.2 Hz, 1H), 7.23-7.27 (m, 1H), 7.44-7.48 (m, 2H), 7.56 (d, *J* = 4.8 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 2H), 11.81 (br s, 1H); ¹³C NMR (DMSO-*d*₆, 100 MHz) δ : 14.1, 27.4, 35.1, 49.2, 77.3, 79.2, 118.9, 126.1, 127.8, 129.0, 129.6, 130.7, 131.8, 137.5, 158.8, 169.3, 193.8, 205.9; HRMS (ESI-TOF) *m/z*: Calcd. for C₂₀H₁₇N₃NaO₂S₃ [M+Na]⁺: 450.0375; Found: 450.0378.

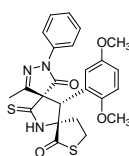


3k: Light yellow solid, m.p. 262.1-263.1 °C; yield 82%, 40.1 mg, 97% ee, >20:1 dr, $[\alpha]_{\text{D}}^{20} = +54.2$ (*c* 2.9, CHCl₃); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{\text{major}} = 12.07$ min; $\tau_{\text{minor}} = 6.65$ min); ¹H NMR (DMSO-*d*₆, 400 MHz) δ : 2.23 (s, 3H), 2.62-2.68 (m, 1H), 2.80-2.86 (m, 1H), 2.89-2.94 (m, 1H), 3.39-3.44 (m, 1H), 5.04 (s, 1H), 7.23-7.27 (m, 1H), 7.42-7.46 (m, 2H), 7.50-7.52 (m, 1H), 7.68-7.73 (m, 3H), 7.88 (d, *J* = 8.4 Hz, 1H), 11.91 (br s, 1H); ¹³C NMR (DMSO-*d*₆, 100 MHz) δ : 14.3, 27.7, 34.7, 46.6, 77.6, 78.9, 119.4, 126.4, 127.3, 128.6, 129.6, 130.4, 132.6, 135.5, 136.2, 137.1, 158.8, 169.3, 193.6, 205.4; HRMS (ESI-TOF) *m/z*: Calcd. for C₂₂H₁₇Cl₂N₃NaO₂S₂ [M+Na]⁺: 512.0031; Found: 512.0035.

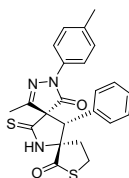


3l: Light yellow solid, m.p. 170.3-171.3 °C; yield 84%, 40.4 mg, 97% ee, >20:1 dr, $[\alpha]_{\text{D}}^{20} =$

+250.5 (*c* 2.9, CHCl₃); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{major} = 38.14$ min; $\tau_{minor} = 13.75$ min); ¹H NMR (DMSO-*d*₆, 400 MHz) δ : 2.12 (s, 3H), 2.45-2.51 (m, 1H), 2.65-2.72 (m, 1H), 2.97-3.04 (m, 1H), 3.24-3.30 (m, 1H), 3.70 (s, 3H), 3.75 (s, 3H), 4.89 (s, 1H), 6.48-6.50 (m, 1H), 6.58 (s, 1H), 7.22-7.26 (m, 1H), 7.43-7.45 (m, 3H), 7.74 (d, *J* = 8.0 Hz, 2H), 11.66 (br s, 1H); ¹³C NMR (DMSO-*d*₆, 100 MHz) δ : 14.0, 27.2, 34.6, 43.9, 55.7, 56.5, 77.4, 78.8, 99.3, 106.0, 110.7, 119.1, 126.1, 129.6, 130.1, 137.5, 159.2, 161.3, 170.1, 194.4, 206.0; HRMS (ESI-TOF) *m/z*: Calcd. for C₂₄H₂₃N₃NaO₄S₂ [M+Na]⁺: 504.1022; Found: 504.1025.

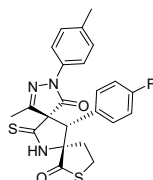


3m: Light yellow solid, m.p. 175.4-176.0 °C; yield 80%, 38.5 mg, 96% ee, >20:1 dr, $[\alpha]_D^{20} = +134.5$ (*c* 2.9, CHCl₃); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{major} = 16.53$ min; $\tau_{minor} = 9.06$ min); ¹H NMR (DMSO-*d*₆, 400 MHz) δ : 2.12 (s, 3H), 2.53-2.56 (m, 1H), 2.68-2.75 (m, 1H), 2.92-2.98 (m, 1H), 3.28-3.32 (m, 1H), 3.35 (s, 3H), 3.51 (s, 3H), 3.70 (s, 3H), 4.94 (s, 1H), 6.88-6.91 (m, 1H), 7.00 (d, *J* = 8.8 Hz, 1H), 7.06 (d, *J* = 2.8 Hz, 1H), 7.23-7.27 (m, 1H), 7.43-7.47 (m, 2H), 7.75 (d, *J* = 8.0 Hz, 2H), 11.73 (br s, 1H); ¹³C NMR (DMSO-*d*₆, 100 MHz) δ : 14.1, 27.3, 34.6, 44.3, 55.7, 56.8, 77.4, 78.8, 113.5, 115.1, 115.5, 118.8, 119.8, 126.1, 129.7, 137.5, 152.0, 153.3, 159.3, 170.1, 194.1, 205.6; HRMS (ESI-TOF) *m/z*: Calcd. for C₂₄H₂₃N₃NaO₄S₂ [M+Na]⁺: 504.1022; Found: 504.1023.

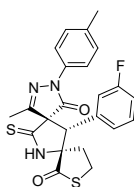


3n: Light yellow solid, m.p. 162.3-162.8 °C; yield 86%, 37.4 mg, >99% ee, >20:1 dr, $[\alpha]_D^{20} = +356.9$ (*c* 2.9, CHCl₃); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{major} = 14.82$ min; $\tau_{minor} = 7.80$ min); ¹H NMR (DMSO-*d*₆, 400 MHz) δ : 2.19 (s, 3H), 2.29 (s, 3H), 2.70-2.80 (m, 2H), 2.80-2.95 (m,

1H), 3.39-3.41 (m, 1H), 4.29 (s, 1H), 7.23 (d, $J = 8.4$ Hz, 2H), 7.32-7.34 (m, 3H), 7.39-7.42 (m, 2H), 7.59 (d, $J = 8.4$ Hz, 2H), 11.84 (br s, 1H); ^{13}C NMR (DMSO- d_6 , 100 MHz) δ : 14.2, 21.0, 27.6, 35.1, 53.6, 77.2, 79.2, 119.2, 129.6, 129.7, 130.0, 130.1, 131.1, 135.0, 135.5, 158.9, 169.6, 194.5, 205.9; HRMS (ESI-TOF) m/z : Calcd. for $\text{C}_{23}\text{H}_{21}\text{N}_3\text{NaO}_2\text{S}_2$ $[\text{M}+\text{Na}]^+$: 458.0967; Found: 458.0965.

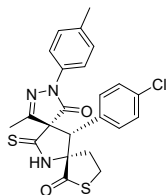


30: Light yellow solid, m.p. 132.3-132.8 °C; yield 87%, 39.4 mg, 96% ee, >20:1 dr, $[\alpha]_{\text{D}}^{20} = +267.8$ (c 2.7, CHCl_3); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{\text{major}} = 13.75$ min; $\tau_{\text{minor}} = 6.64$ min); ^1H NMR (DMSO- d_6 , 400 MHz) δ : 2.20 (s, 3H), 2.29 (s, 3H), 2.72-2.79 (m, 2H), 2.89-2.93 (m, 1H), 3.41-3.45 (m, 1H), 4.31 (s, 1H), 7.17-7.24 (m, 4H), 7.47-7.50 (m, 2H), 7.58 (d, $J = 8.4$ Hz, 2H), 11.84 (br s, 1H); ^{13}C NMR (DMSO- d_6 , 100 MHz) δ : 14.2, 21.0, 27.6, 35.0, 52.5, 77.3, 79.2, 116.5 (d, $J_{\text{CF}} = 22.4$ Hz), 119.3, 127.3 (d, $J_{\text{CF}} = 7.1$ Hz), 130.0, 132.4 (d, $J_{\text{CF}} = 8.4$ Hz), 134.9, 135.6, 158.9, 162.8 (d, $J_{\text{CF}} = 245.2$ Hz), 169.4, 194.3, 205.7; ^{19}F NMR (CDCl_3 , 470 MHz) δ : -112.25; HRMS (ESI-TOF) m/z : Calcd. for $\text{C}_{23}\text{H}_{20}\text{FN}_3\text{NaO}_2\text{S}_2$ $[\text{M}+\text{Na}]^+$: 476.0873; Found: 476.0877.

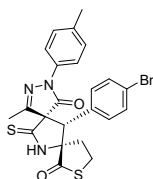


3p: Light yellow solid, m.p. 187.2-187.7 °C; yield 80%, 36.2 mg, 91% ee, >20:1 dr, $[\alpha]_{\text{D}}^{20} = +9.3$ (c 2.9, CHCl_3); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{\text{major}} = 10.55$ min; $\tau_{\text{minor}} = 5.94$ min); ^1H NMR (DMSO- d_6 , 400 MHz) δ : 2.24 (s, 3H), 2.31 (s, 3H), 2.73-2.85 (m, 2H), 2.94-2.99 (m, 1H), 3.44-3.49 (m, 1H), 4.38 (s, 1H), 7.20-7.32 (m, 5H), 7.40-7.43 (m, 1H), 7.62 (d, $J = 8.4$ Hz, 2H), 11.92 (br s, 1H); ^{13}C NMR (DMSO- d_6 , 100 MHz) δ : 14.2, 20.9, 27.7, 35.1, 52.6, 77.2, 79.2, 116.7 (d, $J_{\text{CF}} = 20.4$ Hz), 117.1 (d, $J_{\text{CF}} = 23.1$ Hz), 119.1, 126.4, 130.0, 131.7, 133.6, 134.9, 135.6,

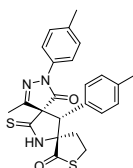
159.0, 162.7 (d, $J_{CF} = 245.0$ Hz), 169.5, 194.2, 205.5; ^{19}F NMR (CDCl_3 , 470 MHz) δ : -111.45; HRMS (ESI-TOF) m/z : Calcd. for $\text{C}_{23}\text{H}_{20}\text{FN}_3\text{NaO}_2\text{S}_2$ $[\text{M}+\text{Na}]^+$: 476.0873; Found: 476.0873.



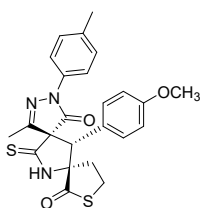
3q: Light yellow solid, m.p. 187.7-188.1 °C; yield 86%, 40.3 mg, >99% ee, >20:1 dr, $[\alpha]_{\text{D}}^{20} = +299.4$ (c 2.9, CHCl_3); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{\text{major}} = 15.15$ min; $\tau_{\text{minor}} = 6.37$ min); ^1H NMR ($\text{DMSO-}d_6$, 400 MHz) δ : 2.20 (s, 3H), 2.28 (s, 3H), 2.69-2.81 (m, 2H), 2.90-2.95 (m, 1H), 3.41-3.46 (m, 1H), 4.31 (s, 1H), 7.22 (d, $J = 8.4$ Hz, 2H), 7.40-7.46 (m, 4H), 7.59 (d, $J = 8.4$ Hz, 2H), 11.86 (br s, 1H); ^{13}C NMR ($\text{DMSO-}d_6$, 100 MHz) δ : 14.2, 21.0, 27.7, 35.0, 52.6, 72.2, 79.2, 119.3, 129.7, 130.0, 130.1, 132.1, 134.7, 134.9, 135.6, 158.9, 169.4, 194.2, 205.6; HRMS (ESI-TOF) m/z : Calcd. for $\text{C}_{23}\text{H}_{20}\text{ClN}_3\text{NaO}_2\text{S}_2$ $[\text{M}+\text{Na}]^+$: 492.0578; Found: 492.0577.



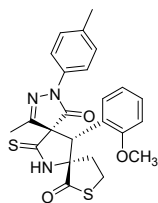
3r: Light yellow solid, m.p. 148.3-149.1 °C; yield 80%, 41.0 mg, 93% ee, >20:1 dr, $[\alpha]_{\text{D}}^{20} = +225.9$ (c 2.1, CHCl_3); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{\text{major}} = 18.14$ min; $\tau_{\text{minor}} = 8.12$ min); ^1H NMR ($\text{DMSO-}d_6$, 400 MHz) δ : 2.12 (s, 3H), 2.23 (s, 3H), 2.62-2.75 (m, 2H), 2.81-2.87 (m, 1H), 3.33-3.39 (m, 1H), 4.21 (s, 1H), 7.16 (d, $J = 8.4$ Hz, 2H), 7.30 (d, $J = 8.4$ Hz, 2H), 7.48-7.52 (m, 4H), 11.79 (br s, 1H); ^{13}C NMR ($\text{DMSO-}d_6$, 100 MHz) δ : 14.2, 21.0, 27.7, 35.0, 52.6, 77.1, 79.1, 119.3, 123.4, 130.0, 130.4, 132.4, 132.6, 134.9, 135.6, 158.9, 169.4, 194.2, 205.6; HRMS (ESI-TOF) m/z : Calcd. for $\text{C}_{23}\text{H}_{20}\text{BrN}_3\text{NaO}_2\text{S}_2$ $[\text{M}+\text{Na}]^+$: 536.0073; Found: 536.0074.



3s: Light yellow solid, m.p. 164.5-165.3 °C; yield 90%, 40.4 mg, 93% ee, >20:1 dr, $[\alpha]_{\text{D}}^{20} = +272.4$ (*c* 2.0, CHCl₃); The ee was determined by HPLC analysis using a Chiralpak IC column (80/20 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{\text{major}} = 9.68$ min; $\tau_{\text{minor}} = 5.79$ min); ¹H NMR (CDCl₃, 400 MHz) δ : 2.16 (s, 3H), 2.19 (s, 3H), 2.26 (s, 3H), 2.55-2.63 (m, 1H), 2.69-2.74 (m, 1H), 3.10-3.24 (m, 2H), 4.34 (s, 1H), 6.98 (d, *J* = 8.0 Hz, 2H), 7.10-7.17 (m, 4H), 7.61 (d, *J* = 8.4 Hz, 2H), 9.76 (br s, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ : 14.1, 21.0, 26.9, 27.7, 34.9, 53.1, 77.4, 79.1, 119.5, 127.4, 129.4, 129.7, 130.0, 135.0, 135.6, 139.3, 157.8, 169.3, 195.9, 204.0; HRMS (ESI-TOF) *m/z*: Calcd. for C₂₄H₂₃N₃NaO₂S₂ [M+Na]⁺: 472.1124; Found: 472.1121.

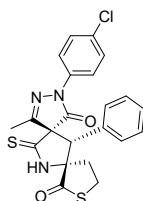


3t: Light yellow solid, m.p. 165.3-165.9 °C; yield 90%, 41.9 mg, 95% ee, >20:1 dr, $[\alpha]_{\text{D}}^{20} = +346.1$ (*c* 2.8, CHCl₃); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{\text{major}} = 22.75$ min; $\tau_{\text{minor}} = 9.84$ min); ¹H NMR (DMSO-*d*₆, 400 MHz) δ : 2.18 (s, 3H), 2.29 (s, 3H), 2.69-2.74 (m, 1H), 2.78-2.83 (m, 1H), 2.86-2.91 (m, 1H), 3.39-3.41 (m, 1H), 3.68 (s, 3H), 4.23 (s, 1H), 6.87 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.8 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 11.78 (br s, 1H); ¹³C NMR (DMSO-*d*₆, 100 MHz) δ : 14.2, 21.0, 27.5, 35.0, 53.1, 55.5, 77.4, 79.2, 114.9, 119.1, 122.6, 130.0, 131.4, 135.1, 135.4, 159.0, 160.2, 169.6, 194.6, 206.1; HRMS (ESI-TOF) *m/z*: Calcd. for C₂₄H₂₃N₃NaO₃S₂ [M+Na]⁺: 488.1073; Found: 488.1073.

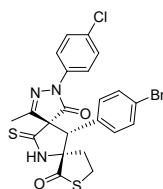


3u: Light yellow solid, m.p. 210.3-210.9 °C; yield 89%, 41.4 mg, 94% ee, >20:1 dr, $[\alpha]_{\text{D}}^{20} = +269.9$ (*c* 2.9, CHCl₃); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{\text{major}} = 22.68$ min; $\tau_{\text{minor}} = 10.65$ min); ¹H NMR (DMSO-*d*₆, 400 MHz) δ : 2.13 (s, 3H), 2.44-2.50 (m, 1H), 2.68-2.75 (m, 1H), 2.94-3.00 (m, 1H), 3.25-3.31 (m, 1H), 3.36 (s, 3H), 3.75 (s, 3H), 4.99 (s, 3H), 6.88-6.92 (m, 1H), 7.05 (d, *J*

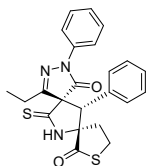
= 8.4 Hz, 1H), 7.22-7.26 (m, 1H), 7.29-7.33 (m, 1H), 7.42-7.46 (m, 2H), 7.51 (d, $J = 7.6$ Hz, 1H), 7.72 (d, $J = 7.6$ Hz, 2H), 11.72 (br s, 1H); ^{13}C NMR (DMSO- d_6 , 100 MHz) δ : 14.1, 27.2, 34.6, 44.1, 56.3, 77.3, 78.9, 112.4, 118.9, 119.1, 121.1, 126.1, 129.3, 129.6, 130.8, 137.4, 158.0, 159.2, 170.1, 194.3, 205.8; HRMS (ESI-TOF) m/z : Calcd. for $\text{C}_{24}\text{H}_{23}\text{N}_3\text{NaO}_3\text{S}_2$ $[\text{M}+\text{Na}]^+$: 488.1073; Found: 488.1077.



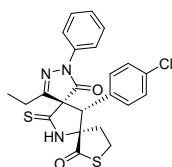
3v: Light yellow solid, m.p. 193.2-193.9 °C; yield 83%, 37.8 mg, 98% ee, >20:1 dr, $[\alpha]_{\text{D}}^{20} = +83.8$ (c 2.9, CHCl_3); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{\text{major}} = 9.61$ min; $\tau_{\text{minor}} = 6.10$ min); ^1H NMR (DMSO- d_6 , 400 MHz) δ : 2.20 (s, 3 H), 2.73-2.79 (m, 2H), 2.87-2.94 (m, 1H), 3.39-3.42 (m, 1H), 4.30 (s, 1H), 7.33-7.39 (m, 5H), 7.50 (d, $J = 8.8$ Hz, 2H), 7.76 (d, $J = 8.8$ Hz, 2H), 11.88 (br s, 1H); ^{13}C NMR (DMSO- d_6 , 100 MHz) δ : 14.2, 27.6, 35.1, 53.5, 77.4, 79.3, 120.5, 129.0, 129.7, 129.8, 129.9, 130.0, 130.1, 130.9, 136.2, 159.6, 169.8, 194.1, 205.8; HRMS (ESI-TOF) m/z : Calcd. for $\text{C}_{22}\text{H}_{18}\text{ClN}_3\text{NaO}_2\text{S}_2$ $[\text{M}+\text{Na}]^+$: 478.0421; Found: 478.0418.



3w: Light yellow solid, m.p. 130.2-131.1 °C; yield 82%, 43.7 mg, 91% ee, 13:1 dr, $[\alpha]_{\text{D}}^{20} = +94.9$ (c 2.9, CHCl_3); The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{\text{major}} = 9.83$ min; $\tau_{\text{minor}} = 5.37$ min); ^1H NMR (DMSO- d_6 , 400 MHz) δ : 2.21 (s, 3H), 2.69-2.74 (m, 1H), 2.77-2.83 (m, 1H), 2.87-2.94 (m, 1H), 3.40-3.46 (m, 1H), 4.30 (s, 1H), 7.36 (d, $J = 8.4$ Hz, 2H), 7.50 (d, $J = 9.2$ Hz, 2H), 7.55 (d, $J = 8.8$ Hz, 2H), 7.75 (d, $J = 8.8$ Hz, 2H), 11.90 (br s, 1H); ^{13}C NMR (DMSO- d_6 , 100 MHz) δ : 14.2, 27.7, 35.0, 52.6, 77.3, 79.2, 120.7, 123.4, 129.7, 130.1, 130.3, 132.3, 132.7, 136.0, 159.6, 169.6, 193.8, 205.5; HRMS (ESI-TOF) m/z : Calcd. for $\text{C}_{22}\text{H}_{17}\text{BrClN}_3\text{NaO}_2\text{S}_2$ $[\text{M}+\text{Na}]^+$: 555.9526; Found: 555.9522.

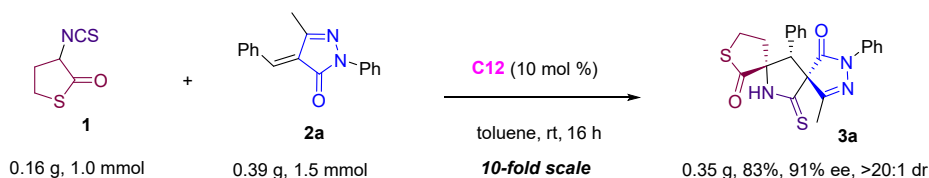


3x: Light yellow solid, m.p. 178.9-179.5 °C; yield 87%, 37.8 mg, 86% ee, >20:1 dr; The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{major} = 7.69$ min; $\tau_{minor} = 5.74$ min); $^1\text{H NMR}$ (DMSO- d_6 , 400 MHz) δ : 1.18-1.22 (m, 3H), 2.48-2.64 (m, 2H), 2.70-2.78 (m, 2H), 2.88-2.95 (m, 1H), 3.42-3.44 (m, 1H), 4.32 (s, 1H), 7.22-7.25 (m, 1H), 7.33-7.46 (m, 7H), 7.75 (d, $J = 8.0$ Hz, 2H), 11.85 (br s, 1H); $^{13}\text{C NMR}$ (DMSO- d_6 , 100 MHz) δ : 9.6, 21.6, 27.6, 35.1, 53.5, 77.5, 79.3, 119.1, 126.2, 129.6, 129.7, 130.1, 131.1, 137.5, 162.6, 169.9, 194.7, 206.0; HRMS (ESI-TOF) m/z : Calcd. for $\text{C}_{23}\text{H}_{21}\text{N}_3\text{NaO}_2\text{S}_2$ $[\text{M}+\text{Na}]^+$: 458.0967; Found: 458.0962.



3y: Light yellow solid, m.p. 184.3-184.6 °C; yield 90%, 42.2 mg, 98% ee, >20:1 dr; The ee was determined by HPLC analysis using a Chiralpak IC column (85/15 hexane/*i*-PrOH; flow rate: 1.0 mL/min; $\lambda = 254$ nm; $\tau_{major} = 7.42$ min; $\tau_{minor} = 4.95$ min); $^1\text{H NMR}$ (DMSO- d_6 , 400 MHz) δ : 1.18-1.22 (m, 3H), 2.47-2.54 (m, 1H), 2.59-2.65 (m, 1H), 2.67-2.73 (m, 1H), 2.76-2.82 (m, 1H), 2.91-2.94 (m, 1H), 3.41-3.43 (m, 1H), 4.33 (s, 1H), 7.22-7.25 (m, 1H), 7.42 (s, 6H), 7.74 (d, $J = 7.2$ Hz, 2H), 11.88 (br s, 1H); $^{13}\text{C NMR}$ (DMSO- d_6 , 100 MHz) δ : 9.6, 21.6, 27.7, 35.0, 52.6, 77.5, 79.2, 119.3, 126.2, 129.6, 129.7, 130.1, 132.1, 134.7, 137.4, 162.6, 169.7, 194.4, 205.7; HRMS (ESI-TOF) m/z : Calcd. for $\text{C}_{23}\text{H}_{20}\text{ClN}_3\text{NaO}_2\text{S}_2$ $[\text{M}+\text{Na}]^+$: 492.0578; Found: 492.0582.

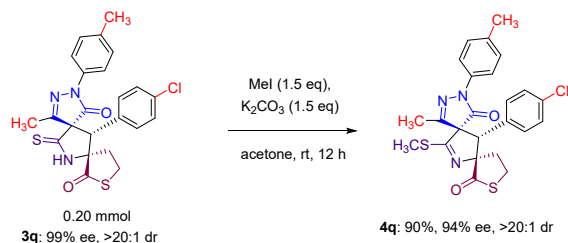
6. Preparative scale synthesis of the product 3a



In a sealed tube equipped with a magnetic stirring bar, to the mixture of 3-isothiocyanatothiobutyl lactone **1** (0.16 g, 1.0 mmol), and squaramide catalyst **C12** (10 mol %) in 15 mL of

freshly distilled toluene was added alkylidene pyrazolone **2** (0.39 g, 1.5 mmol). The reaction mixture was stirred at room temperature for 16 h and was directly loaded onto a silica gel and purified by flash chromatography (hexane/EtOAc, 10/1, v/v) to give the desired product **3a** (0.35 g, 83%, 91% ee, >20:1 dr).

7. Further investigation of transformation of **3q**



To a stirred solution of **3q** (93.8 mg, 0.20 mmol) in acetone (1.0 mL) was added K₂CO₃ (41 mg, 0.30 mmol) at 0 °C. Then iodomethane (43 mg, 0.30 mmol) in 2.0 mL acetone was added dropwise into the stirred reaction mixture. The reaction mixture was allowed to stir at room temperature for another 12 h, and was directly loaded onto a silica gel and purified by flash chromatography (hexane/EtOAc, 10/1, v/v) to give the desired product **4q** (90%, 94% ee, >20:1 dr).

4q: Light yellow solid, m.p. 174.3-175.5 °C; yield 90%, 43.7 mg, 94% ee, >20:1 dr; The ee was determined by HPLC analysis using a Chiralpak IC column (90/10 hexane/*i*-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; τ_{major} = 7.69 min; τ_{minor} = 10.47 min); ¹H NMR (CDCl₃, 400 MHz) δ : 2.24 (s, 3H), 2.28 (s, 3H), 2.48 (s, 3H), 2.84-2.88 (m, 1H), 3.25-3.28 (m, 1H), 3.37-3.38 (m, 1H), 3.53-3.60 (m, 1H), 4.45 (s, 1H), 7.21-7.23 (m, 2H), 7.32-7.39 (m, 4H), 7.55-7.57 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ : 13.8, 14.2, 20.9, 28.7, 37.5, 54.1, 77.1, 89.3, 119.3, 129.5, 130.0, 131.1, 132.3, 134.1, 134.8, 135.8, 157.9, 168.3, 168.5, 206.5; HRMS (ESI-TOF) *m/z*: Calcd. for C₂₄H₂₂ClN₃NaO₂S₂ [M+Na]⁺: 506.0734; Found: 506.0737.

8. X-ray crystal data for compound 3k

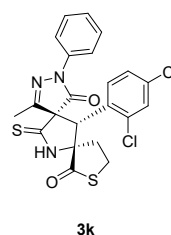
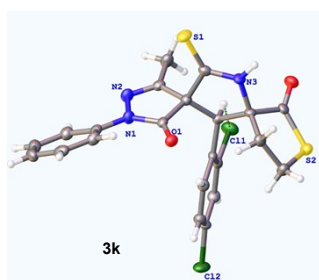


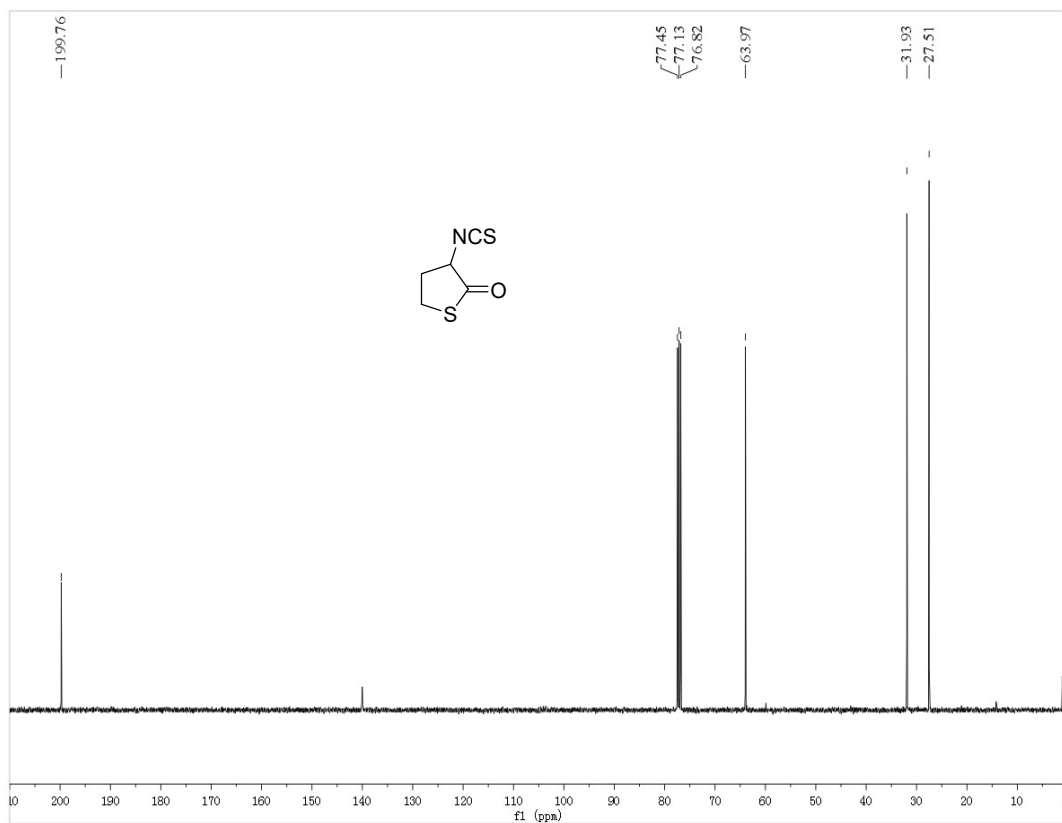
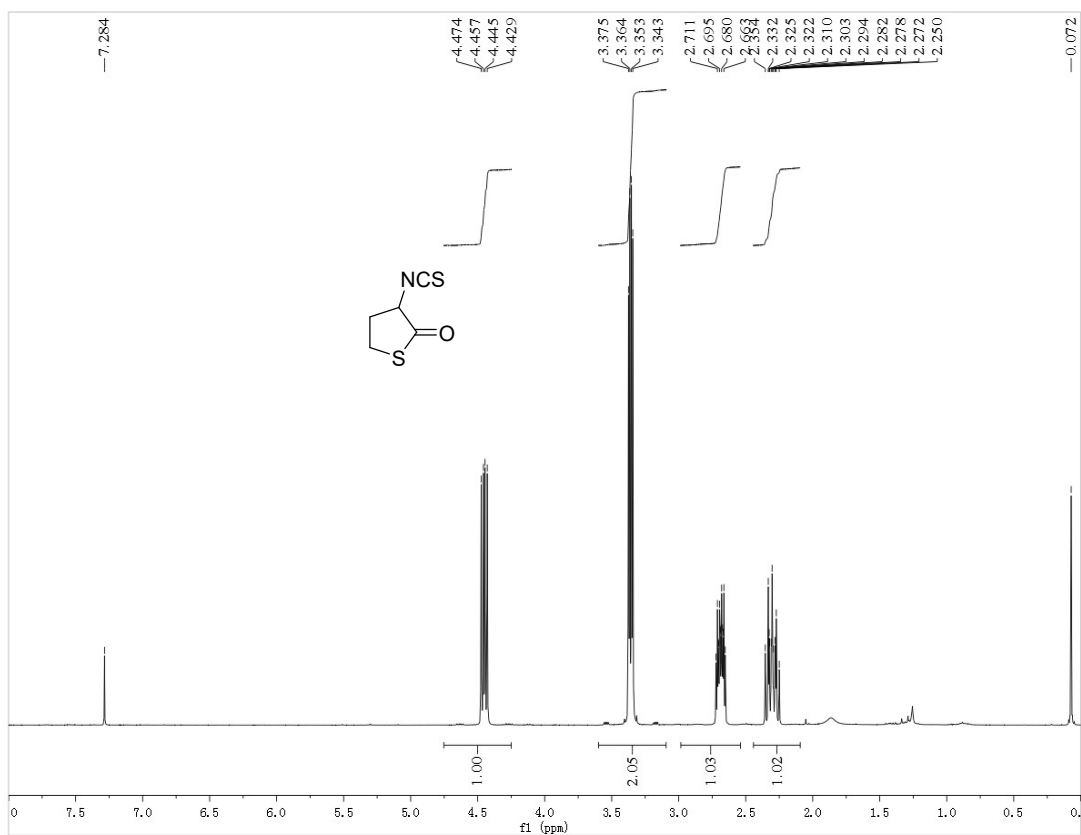
Table S1 Crystal data and structure refinement for 3k

Identification code	3k
Empirical formula	C ₂₂ H ₁₇ Cl ₂ N ₃ O ₂ S ₂
Formula weight	490.40
Temperature/K	169.99(10)
Crystal system	monoclinic
Space group	P2 ₁
a/Å, b/Å, c/Å	9.0271(6), 10.9083(6), 11.1404(8)
α/°, β/°, γ/°	90, 105.790(7), 90.
Volume/Å ³	1055.60(12)
Z	2
ρ _{calc} /cm ³	1.543
μ/mm ⁻¹	0.532
F(000)	504.0
Radiation	Mo Kα (λ = 0.71073)
Crystal size/mm ³	0.15 × 0.12 × 0.11
2θ range for data collection/°	4.69 to 58.856
Index ranges	-10 ≤ h ≤ 11, -14 ≤ k ≤ 14, -11 ≤ l ≤ 15
Reflections collected	5127
Independent reflections	3901 [R _{int} = 0.0231, R _{sigma} = 0.0540]
Data/restraints/parameters	3901/1/281
Goodness-of-fit on F ²	0.978
Final R indexes [I ≥ 2σ (I)]	R ₁ = 0.0359, wR ₂ = 0.0685
Final R indexes [all data]	R ₁ = 0.0416, wR ₂ = 0.0709
Largest diff. peak/hole / e Å ⁻³	0.26/-0.23
Flack/Hoof parameter	-0.01(4)/0.00(5)

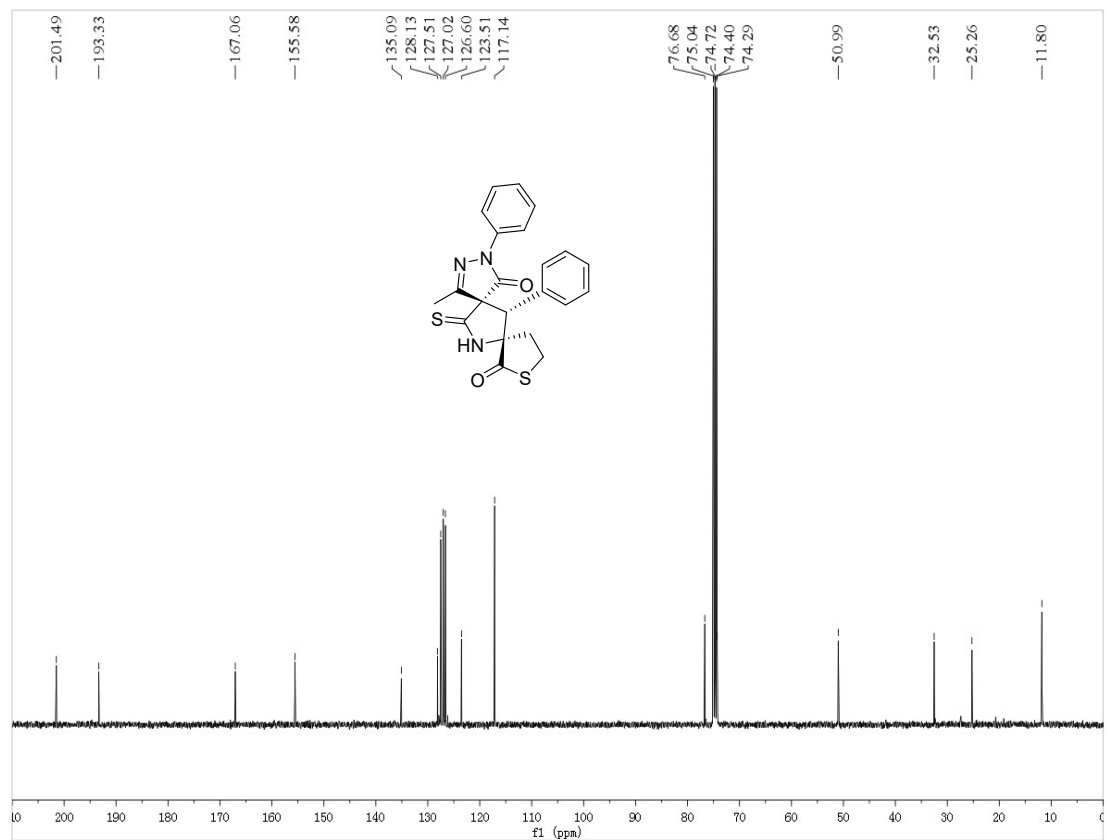
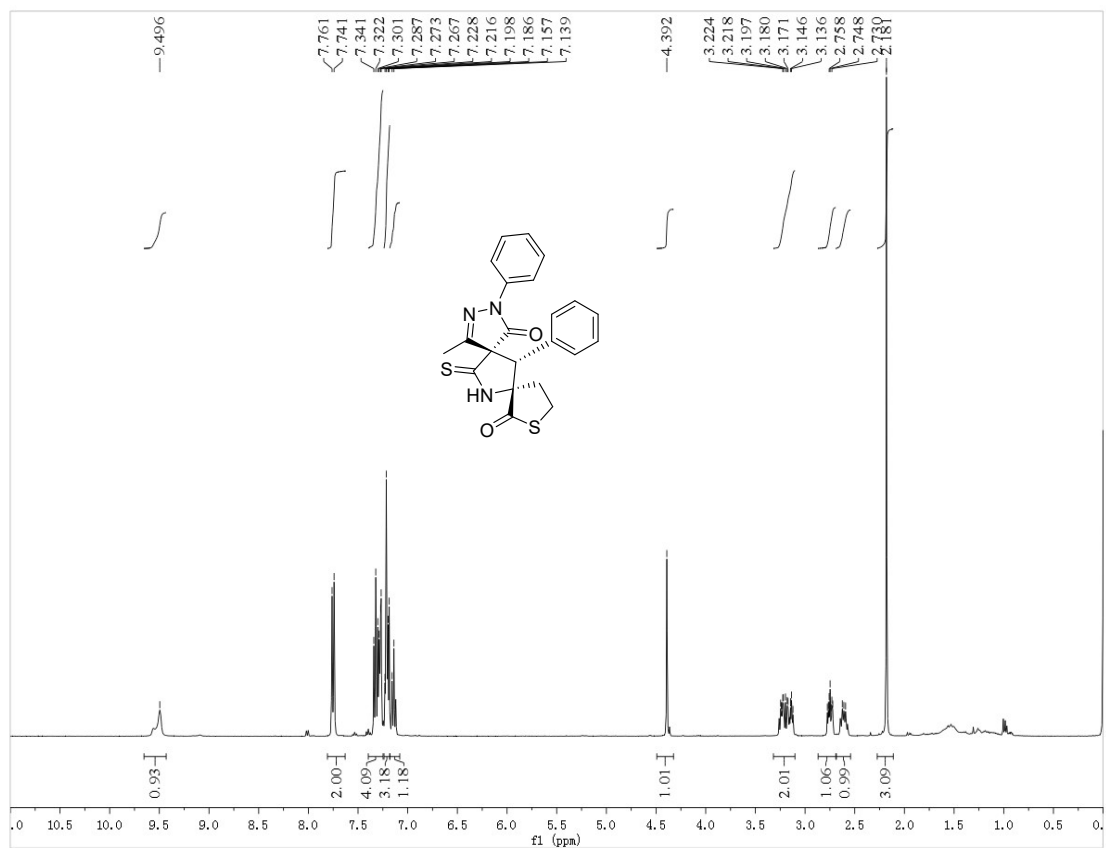
Crystal Data for C₂₂H₁₇Cl₂N₃O₂S₂ (*M* = 490.40 g/mol): monoclinic, space group P2₁ (no. 4), *a* = 9.0271(6) Å, *b* = 10.9083(6) Å, *c* = 11.1404(8) Å, β = 105.790(7)°, *V* = 1055.60(12) Å³, *Z* = 2, *T* = 169.99(10) K, μ(Mo Kα) = 0.532 mm⁻¹, *D*_{calc} = 1.543 g/cm³, 5127 reflections measured (4.69° ≤ 2θ ≤ 58.856°), 3901 unique (*R*_{int} = 0.0231, *R*_{sigma} = 0.0540) which were used in all calculations. The final *R*₁ was 0.0359 (*I* > 2σ(*I*)) and *wR*₂ was 0.0709 (all data).

9. The Copies of ^1H NMR, ^{13}C NMR and HPLC Spectra for Compounds 1, 3 and 4

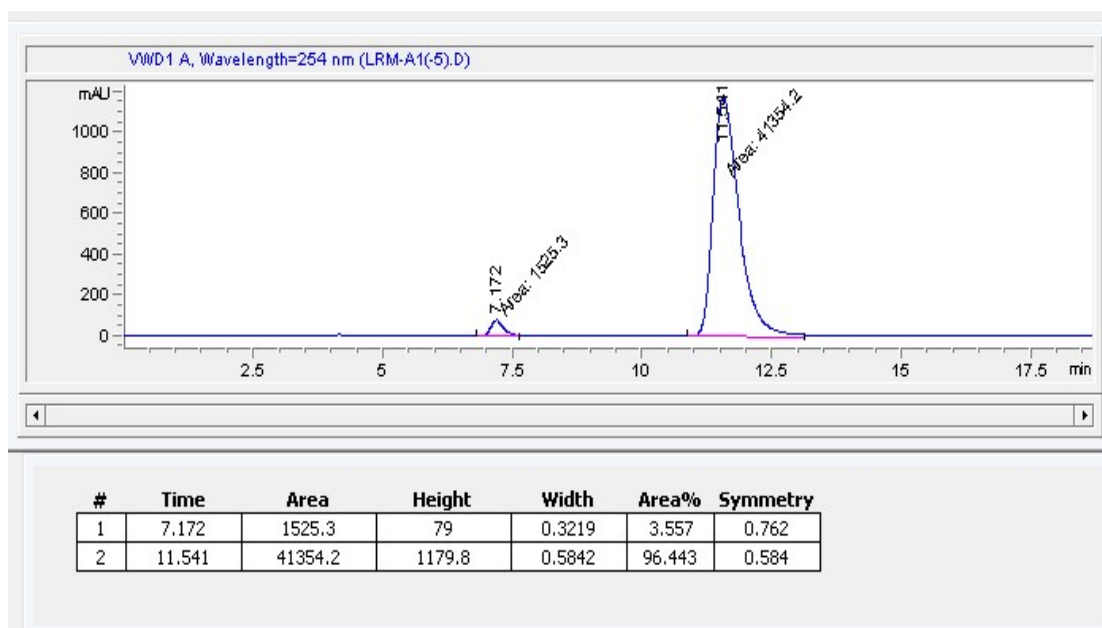
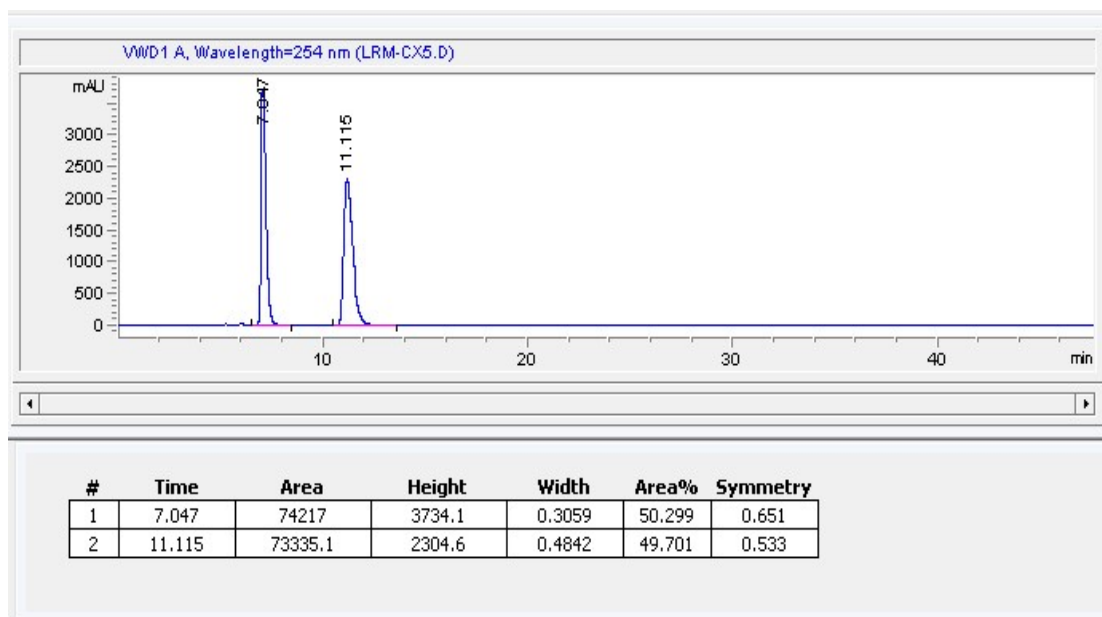
^1H and ^{13}C NMR of 1



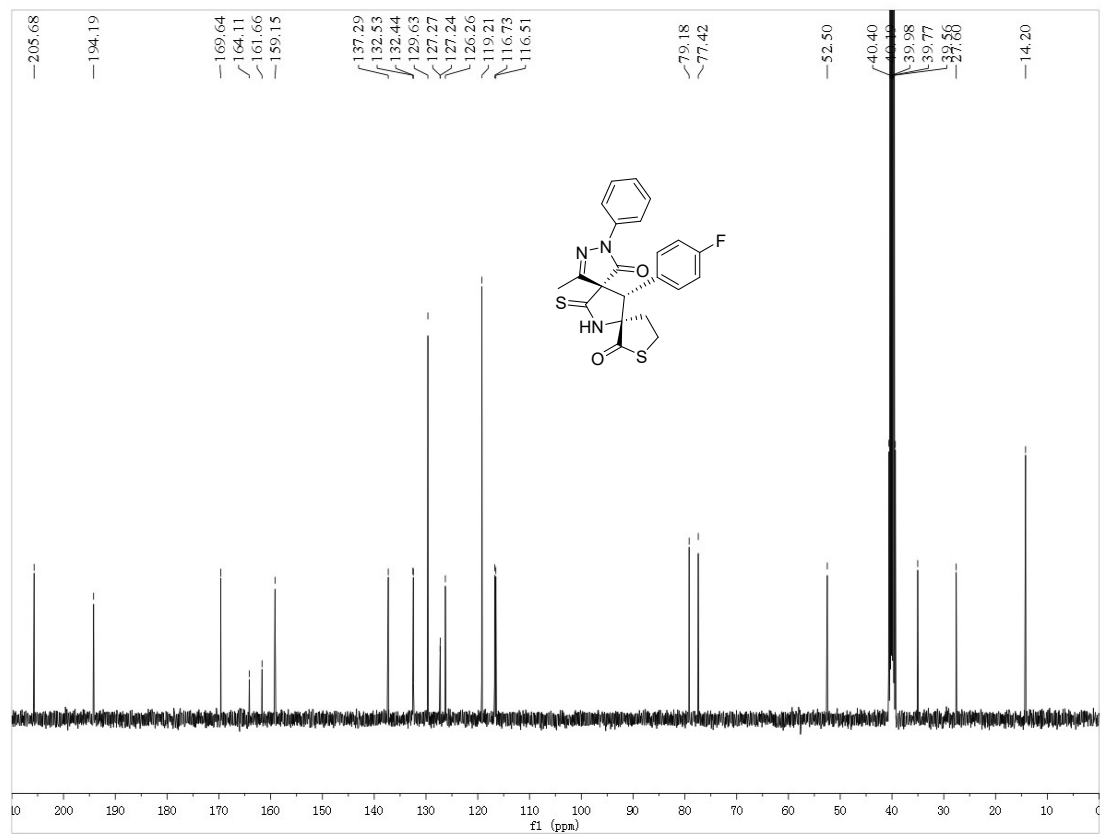
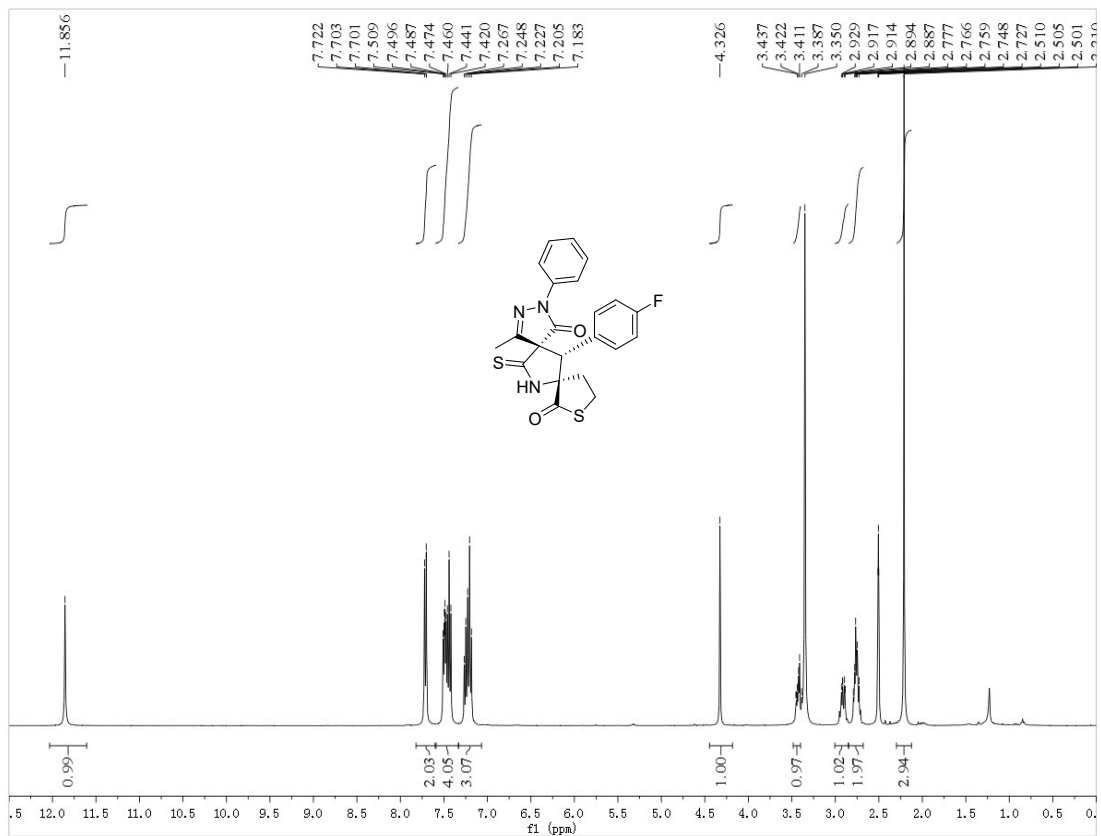
^1H and ^{13}C NMR of 3a



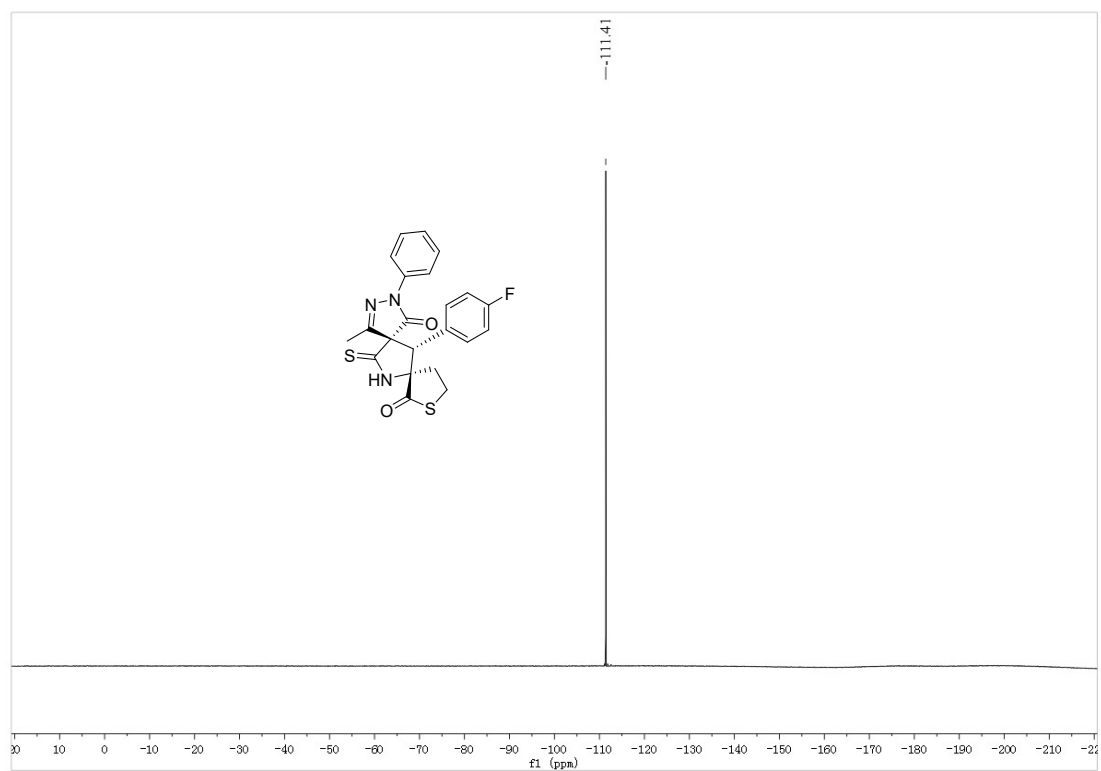
HPLC of 3a



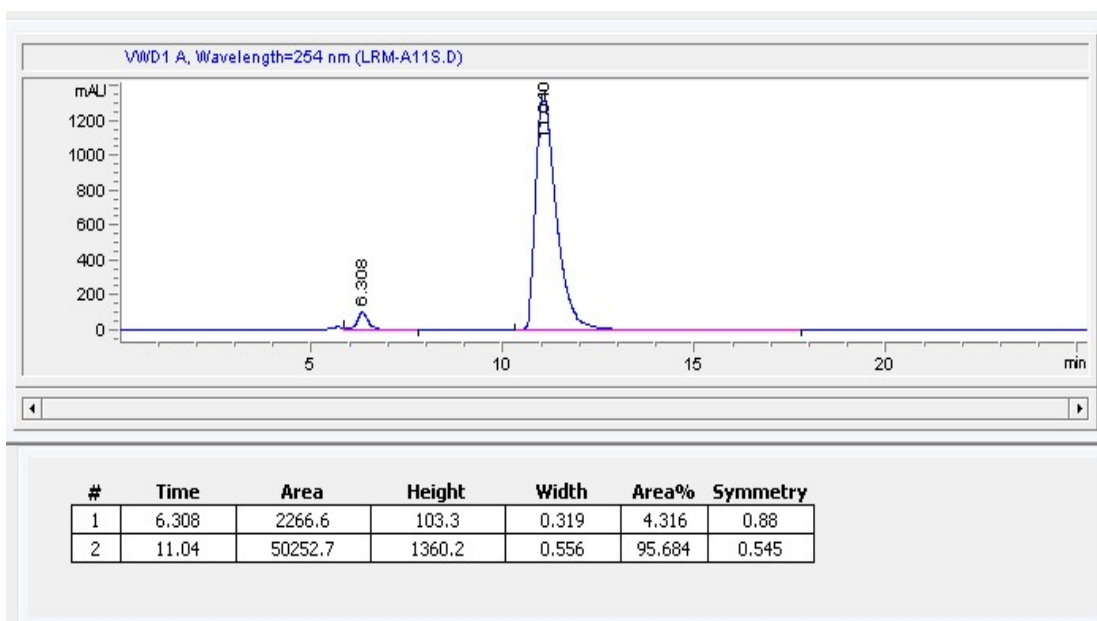
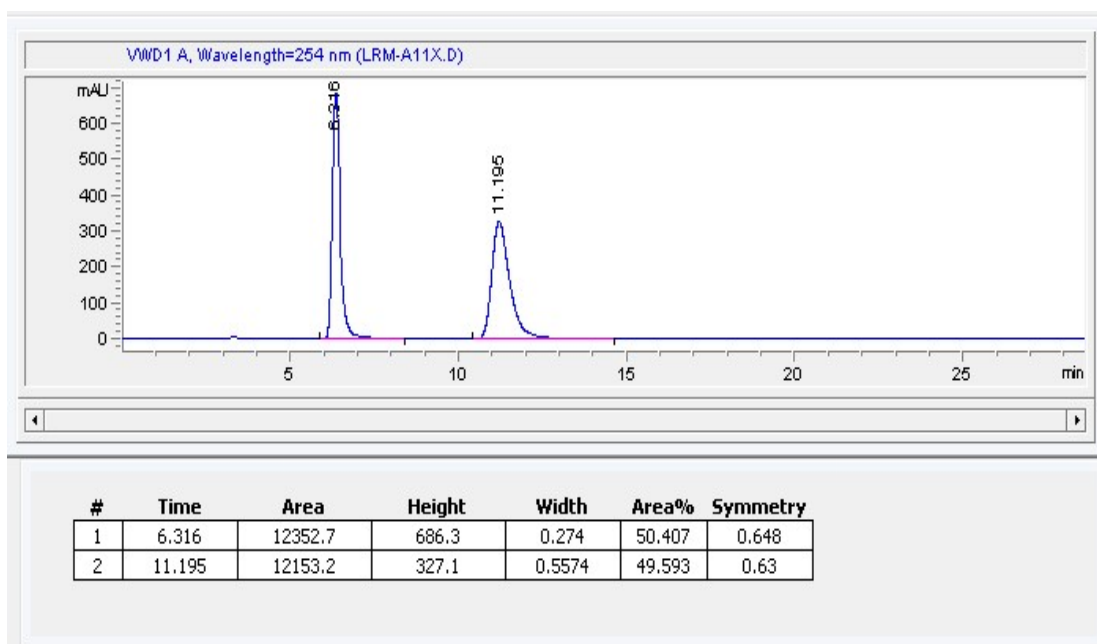
¹H and ¹³C NMR of 3b



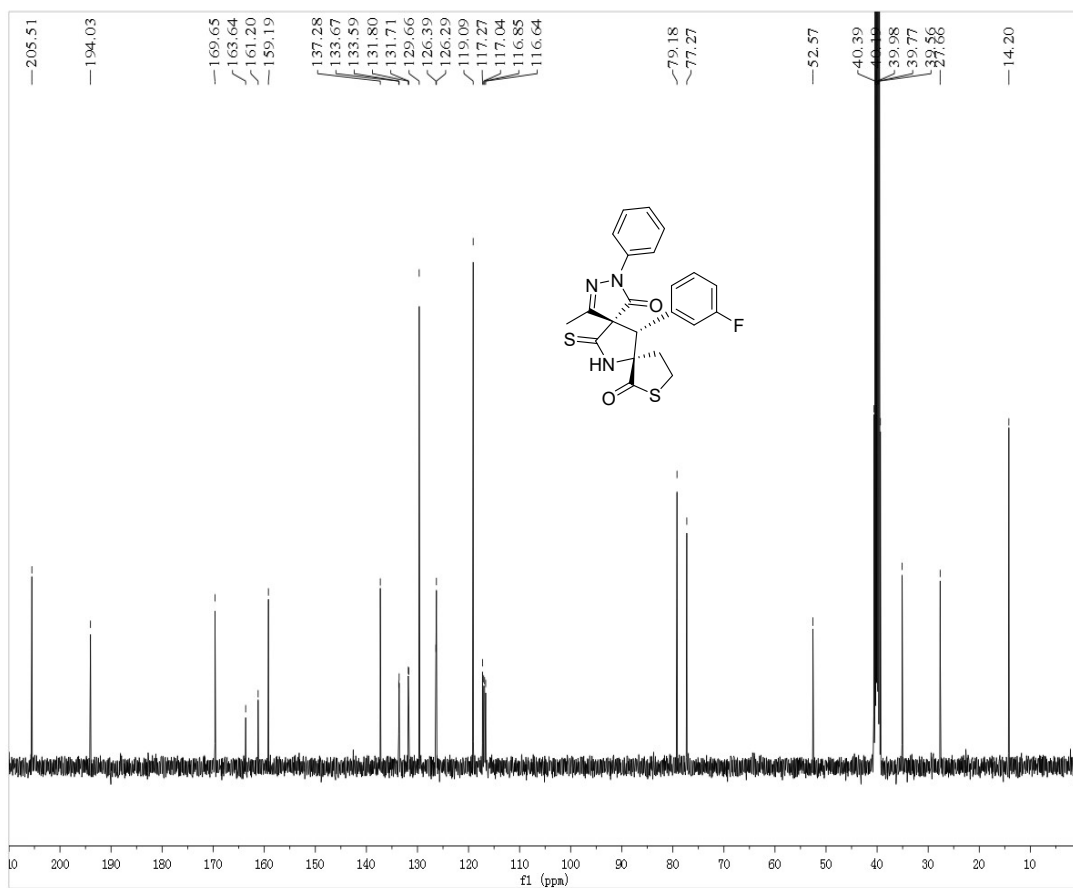
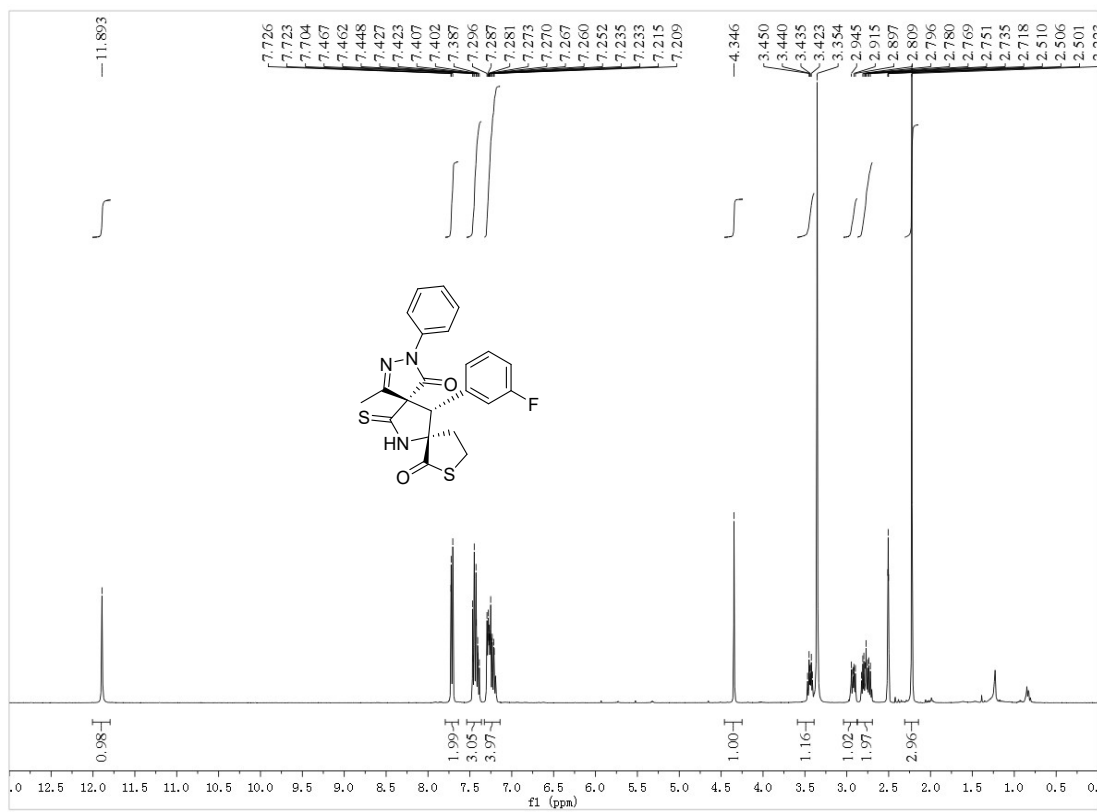
¹⁹F NMR of 3b



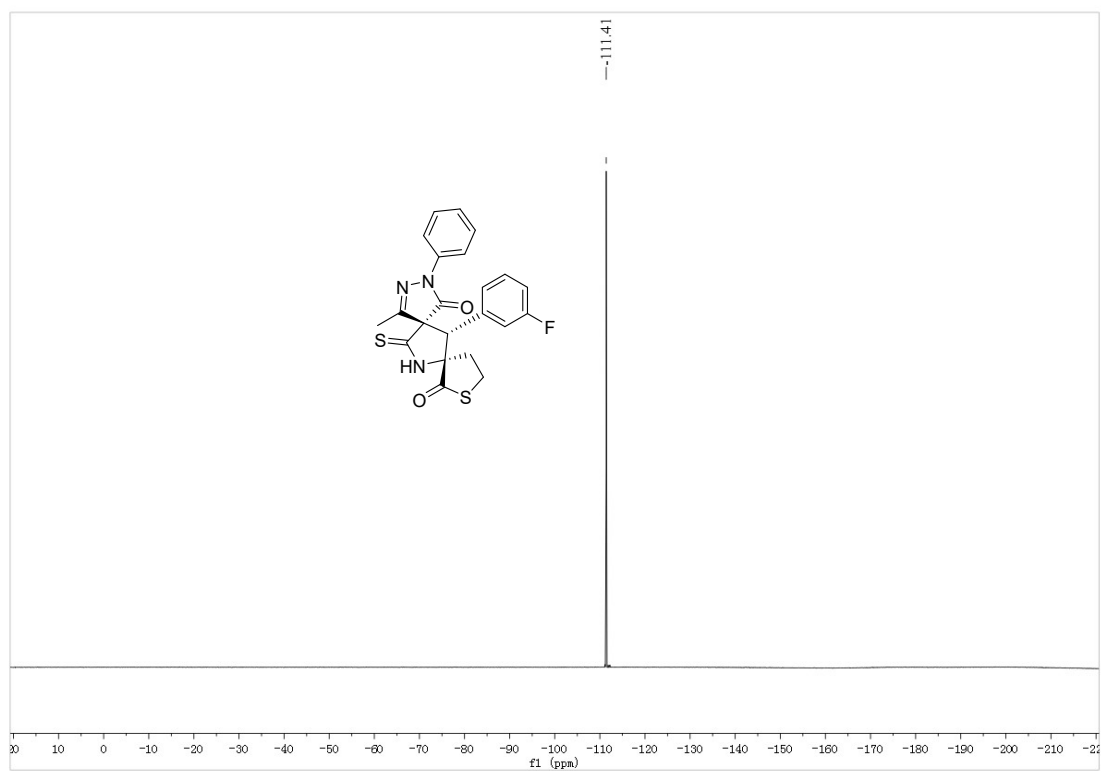
HPLC of 3b



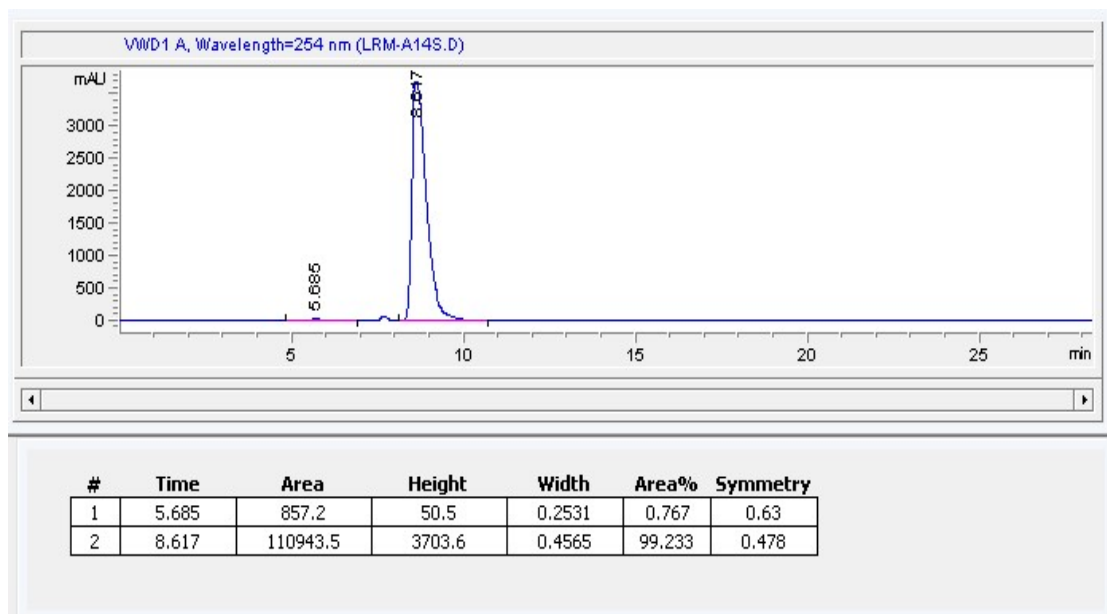
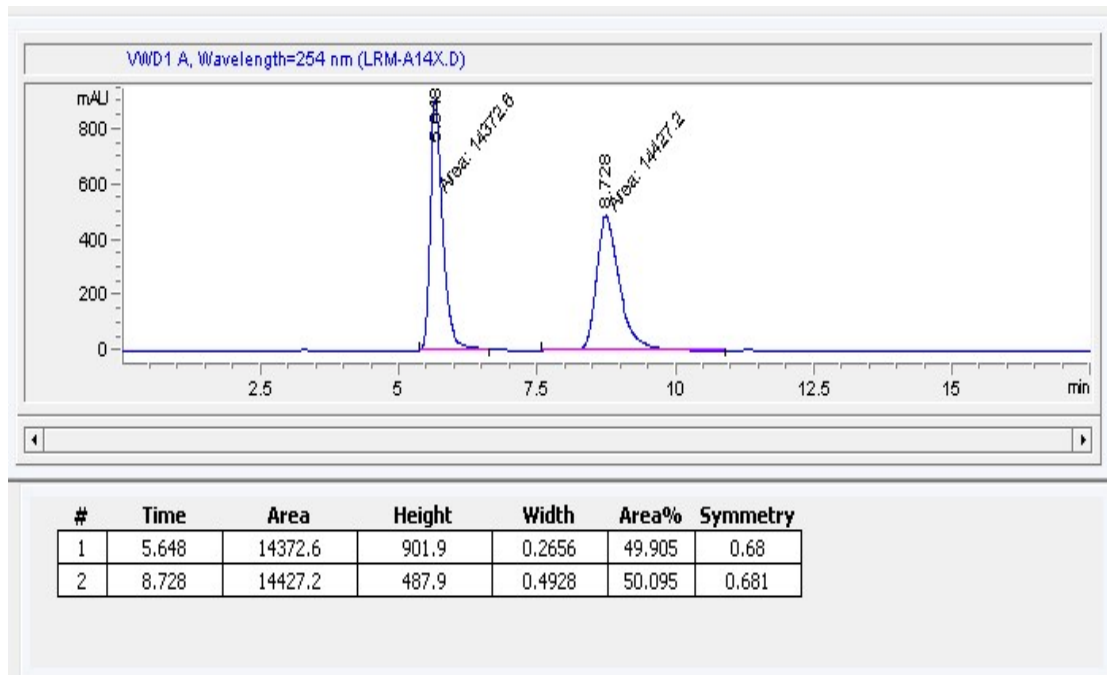
¹H and ¹³C NMR of 3c



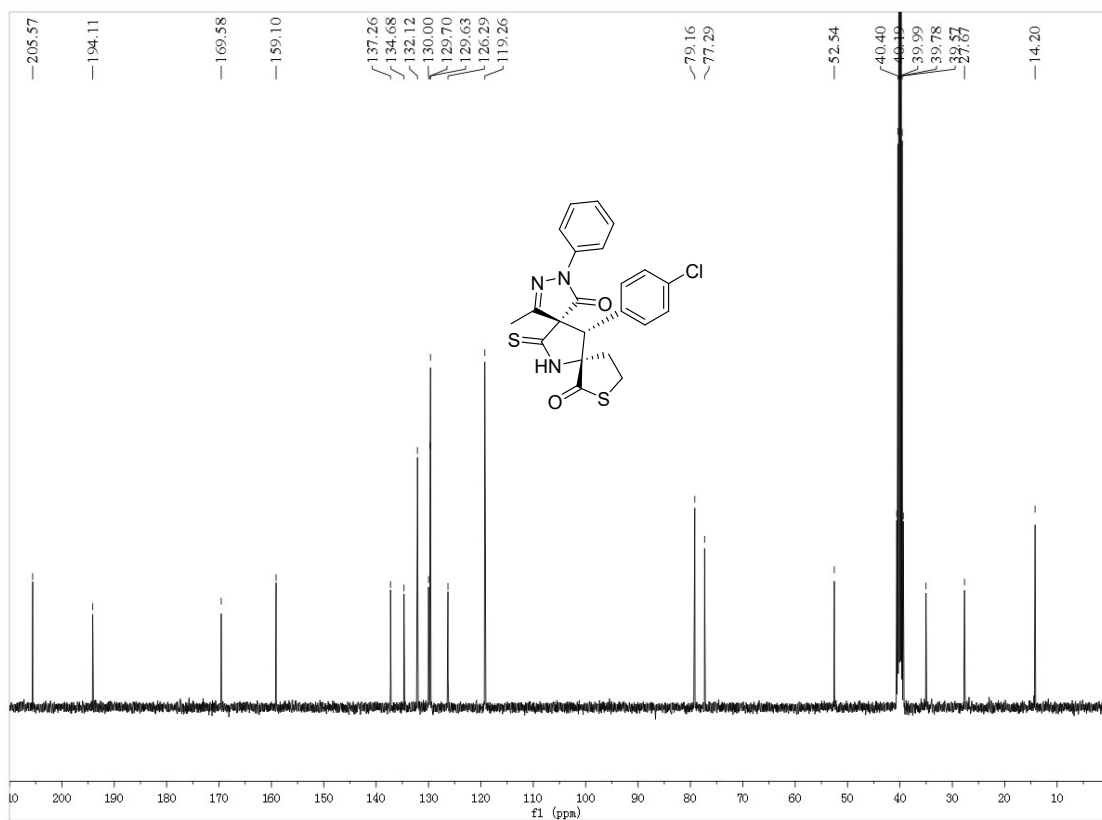
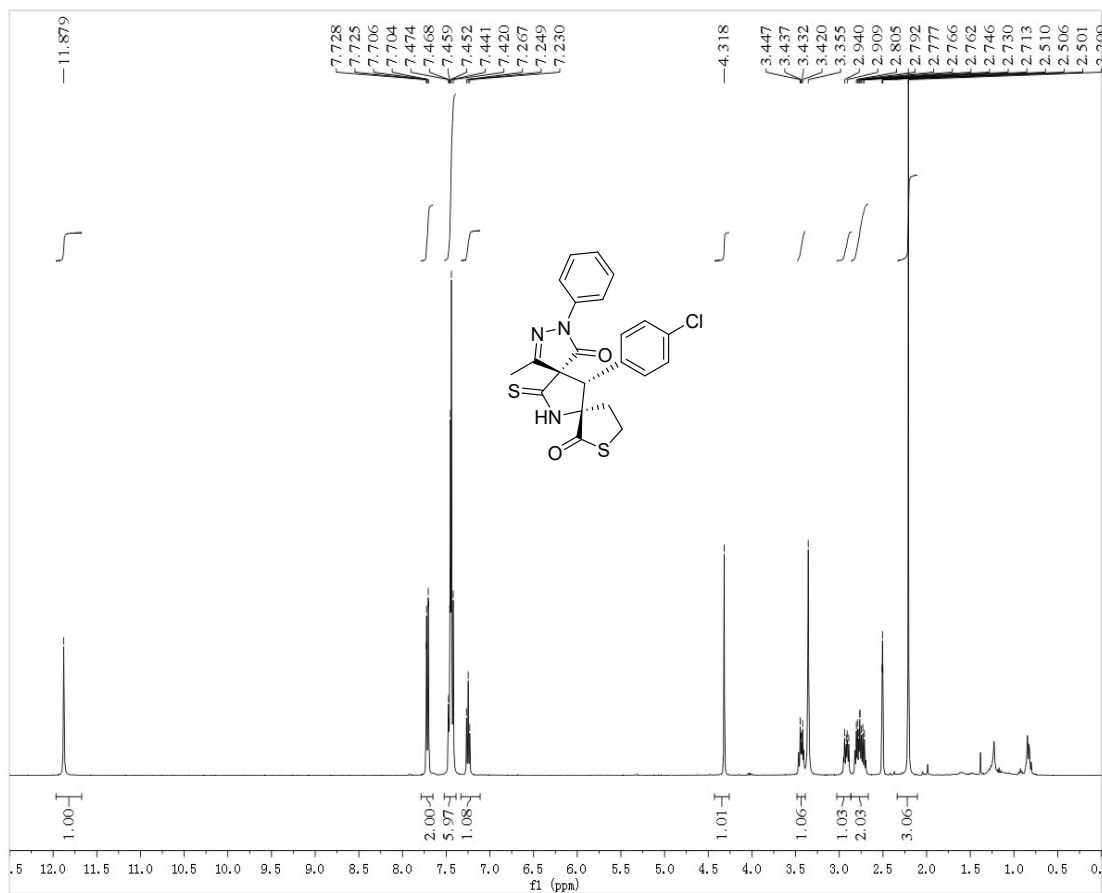
¹⁹F NMR of 3c



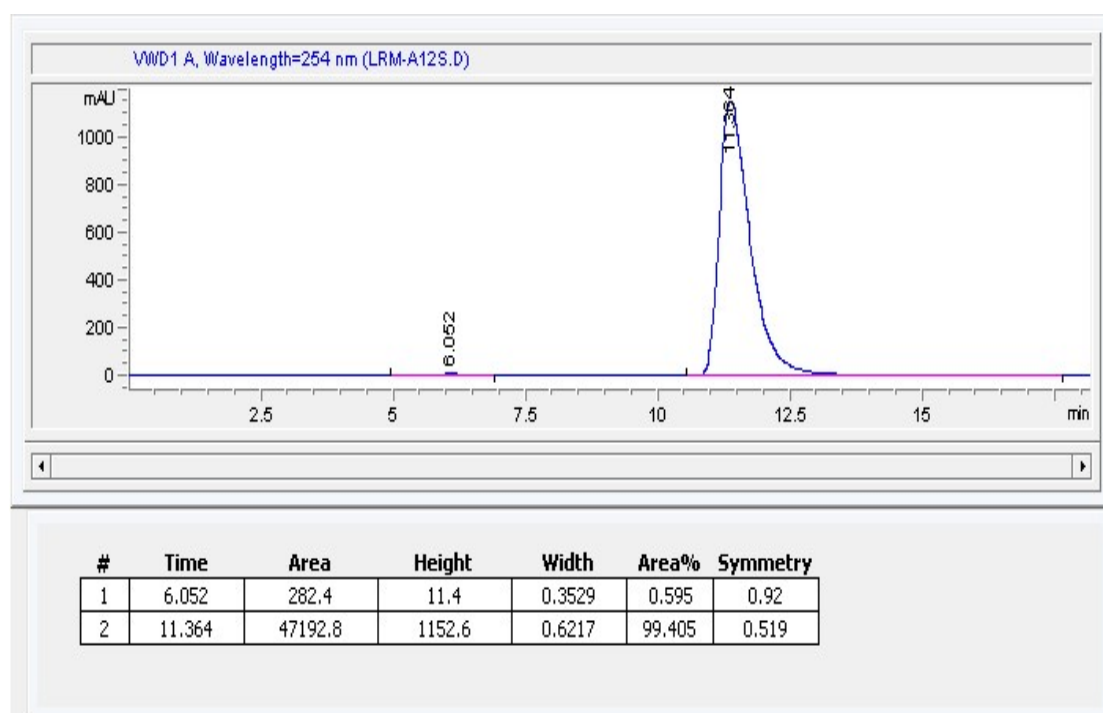
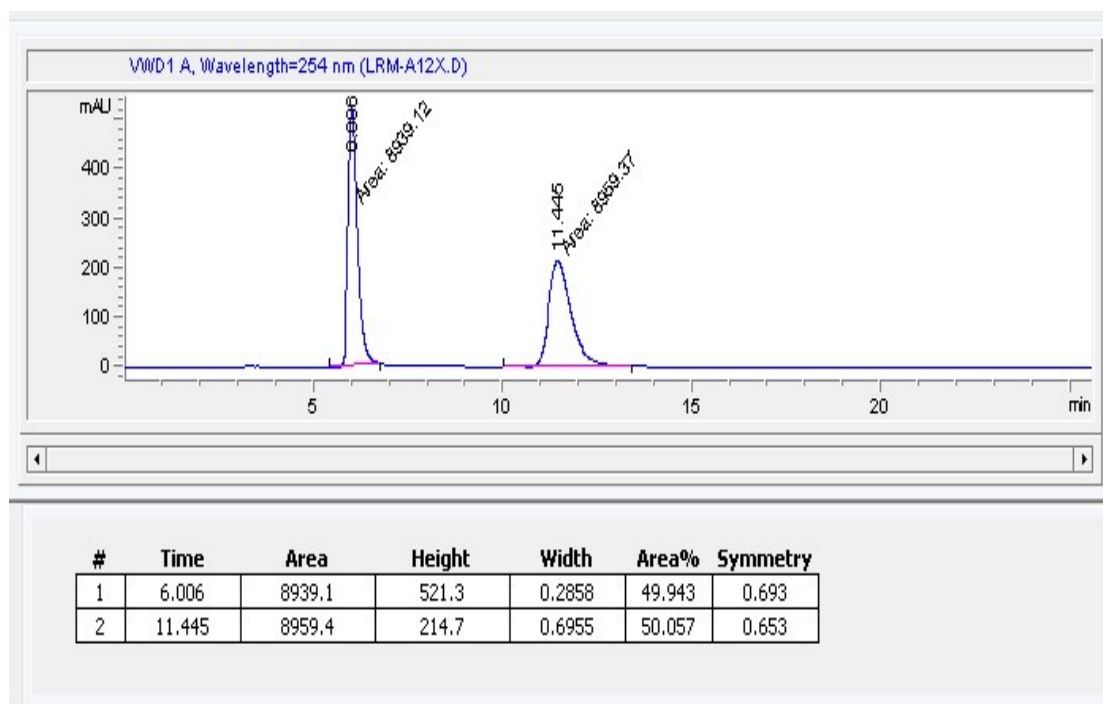
HPLC of 3c



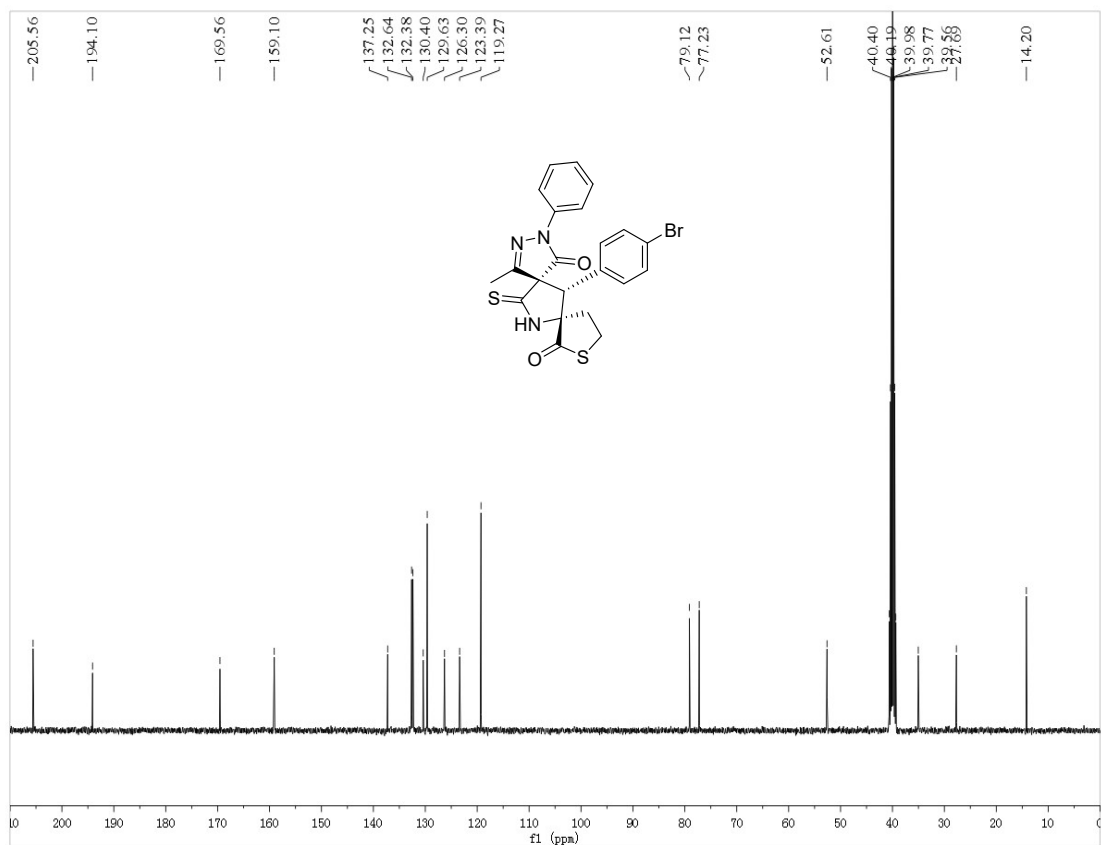
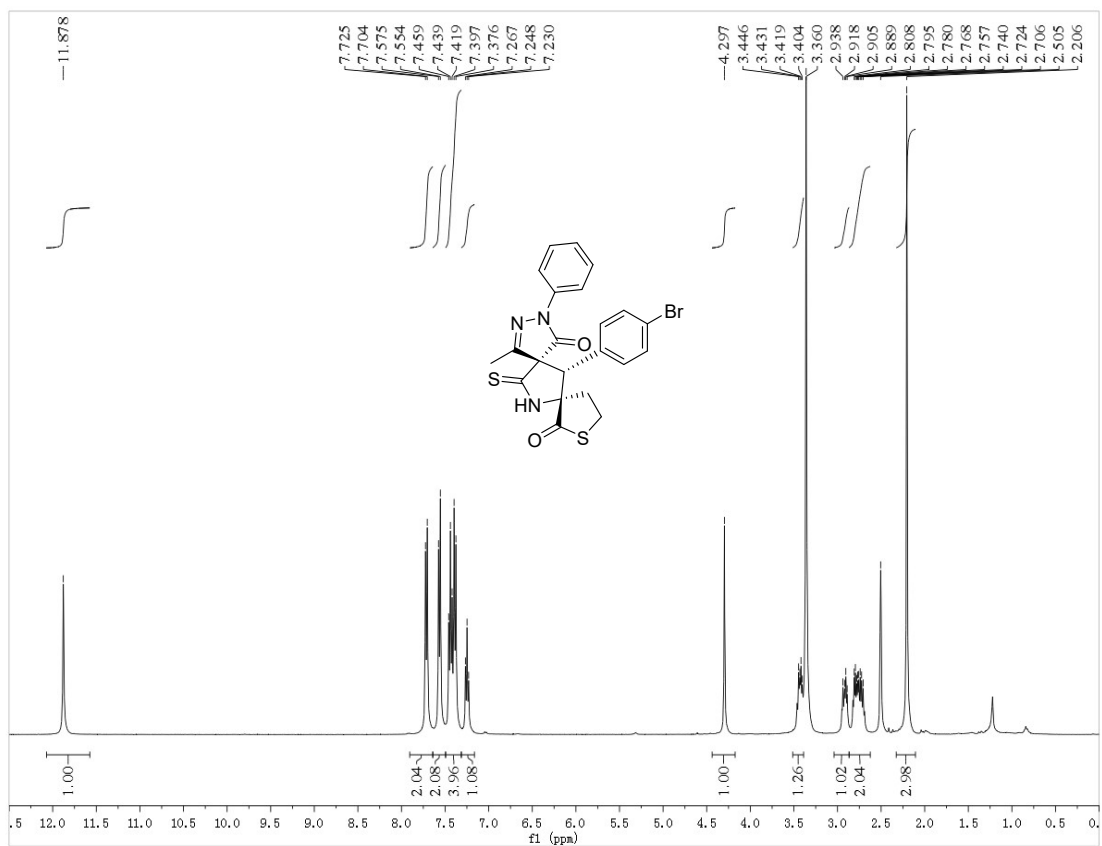
¹H and ¹³C NMR of 3d



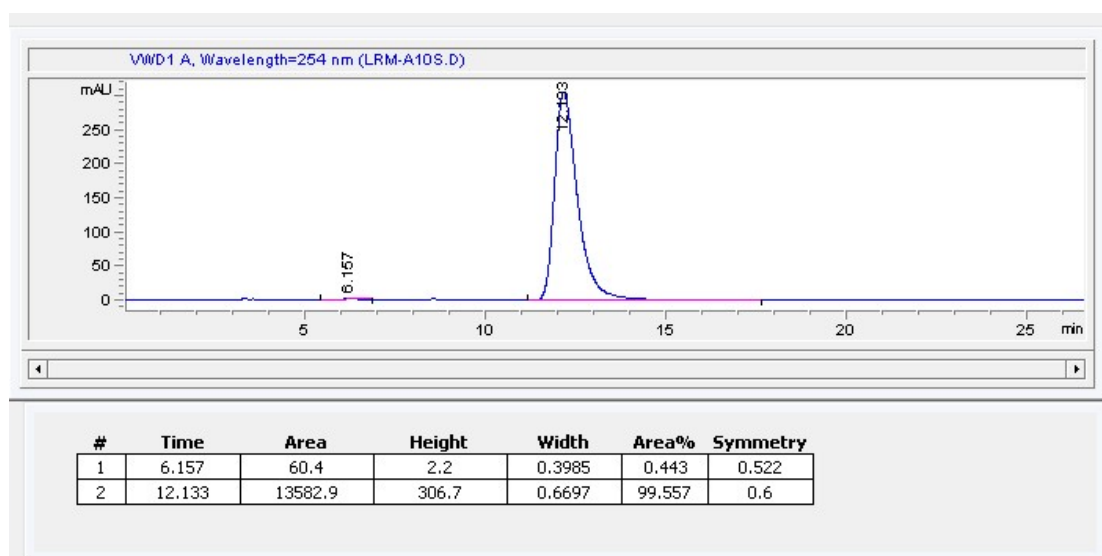
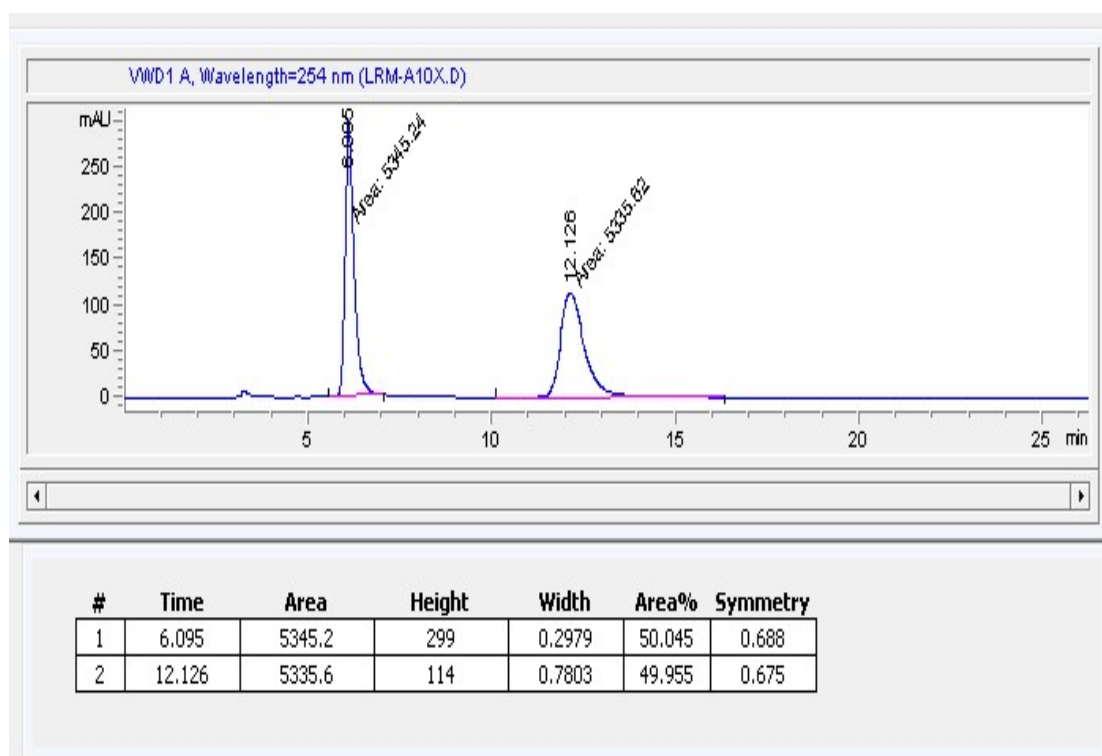
HPLC of 3d



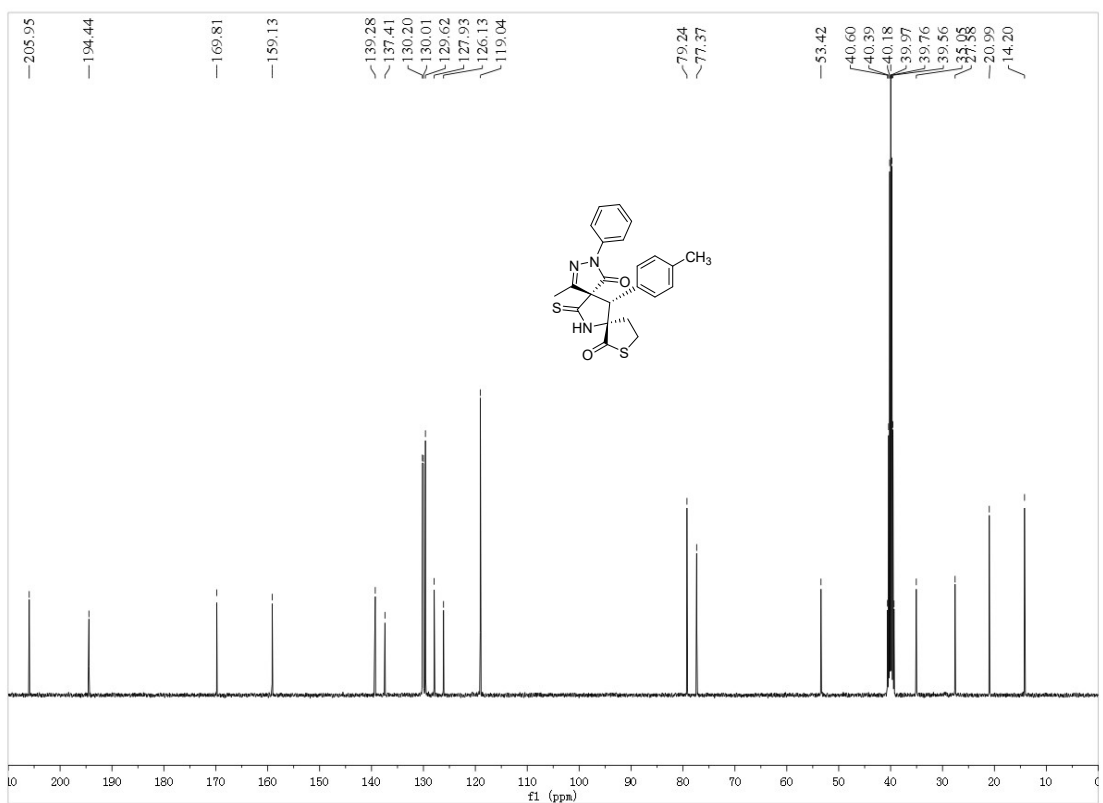
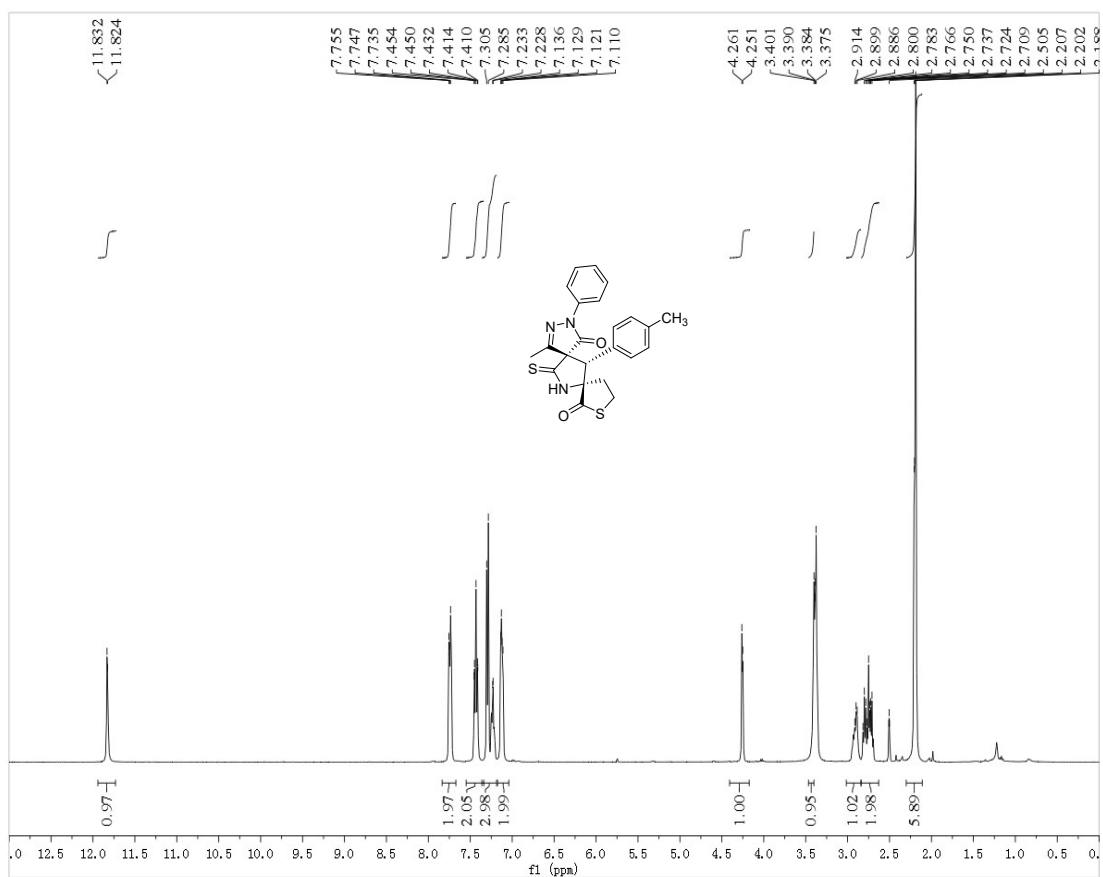
¹H and ¹³C NMR of 3e



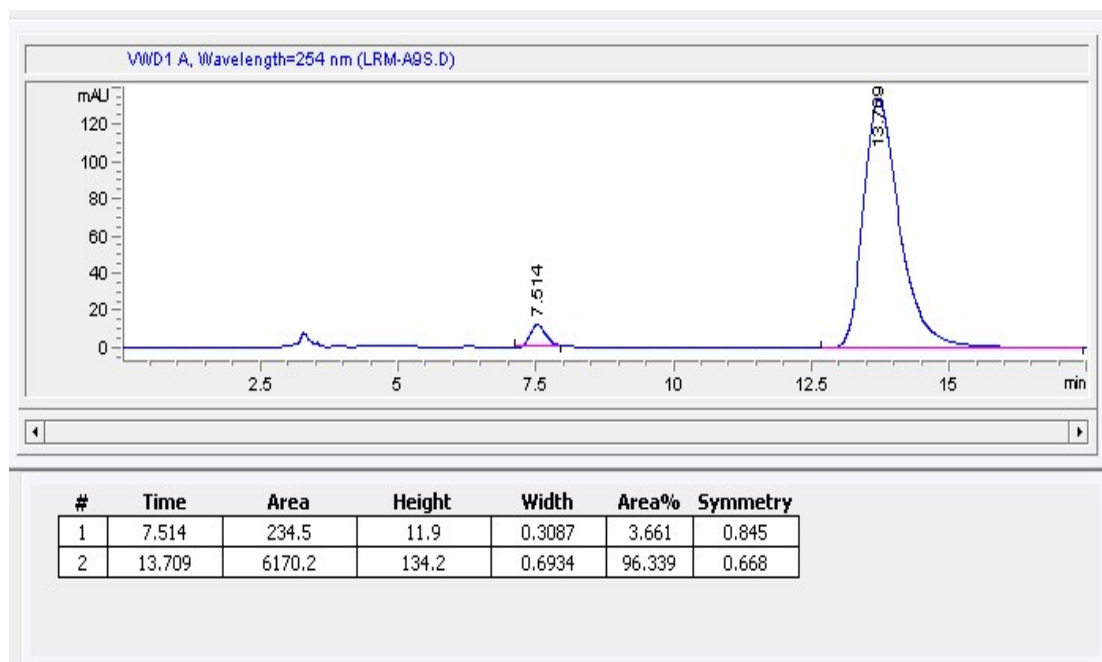
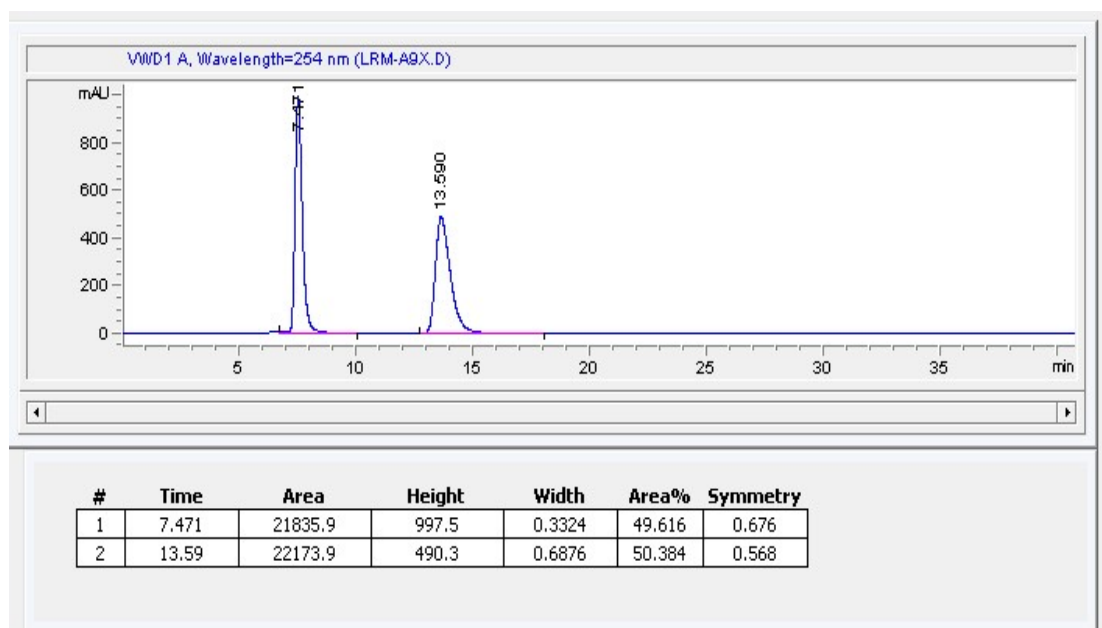
HPLC of 3e



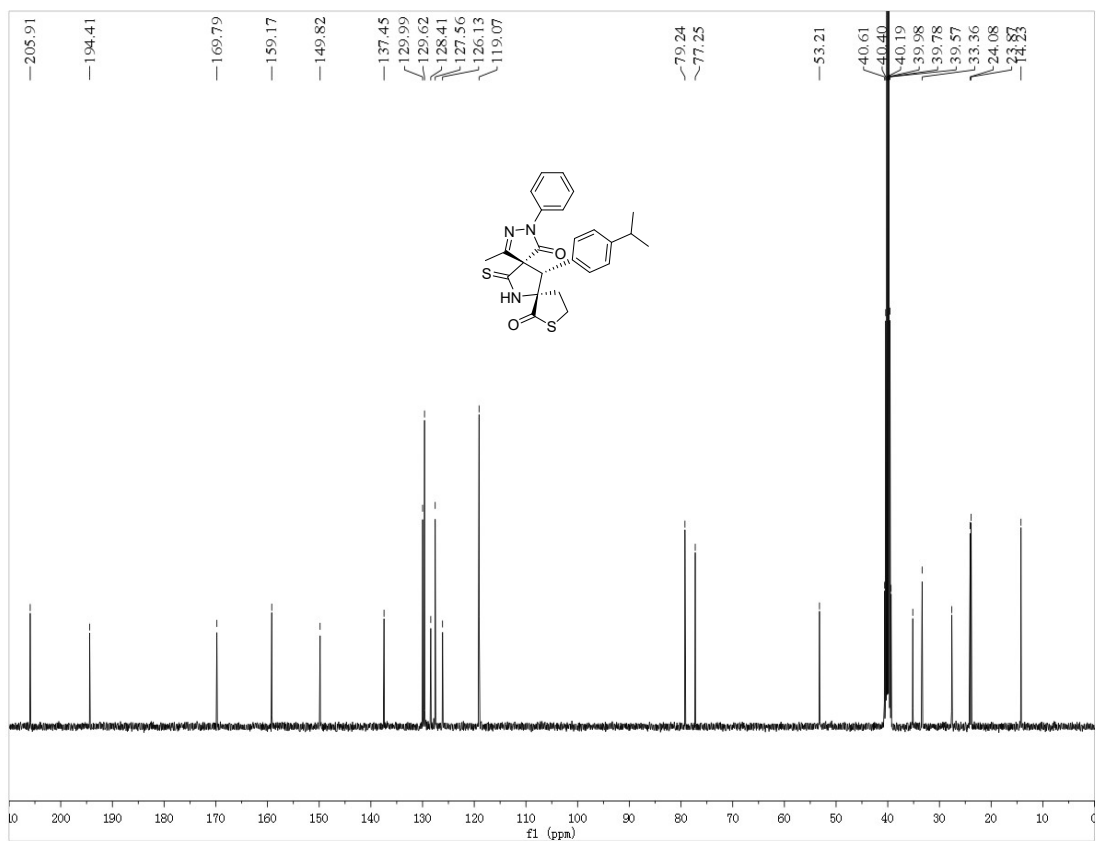
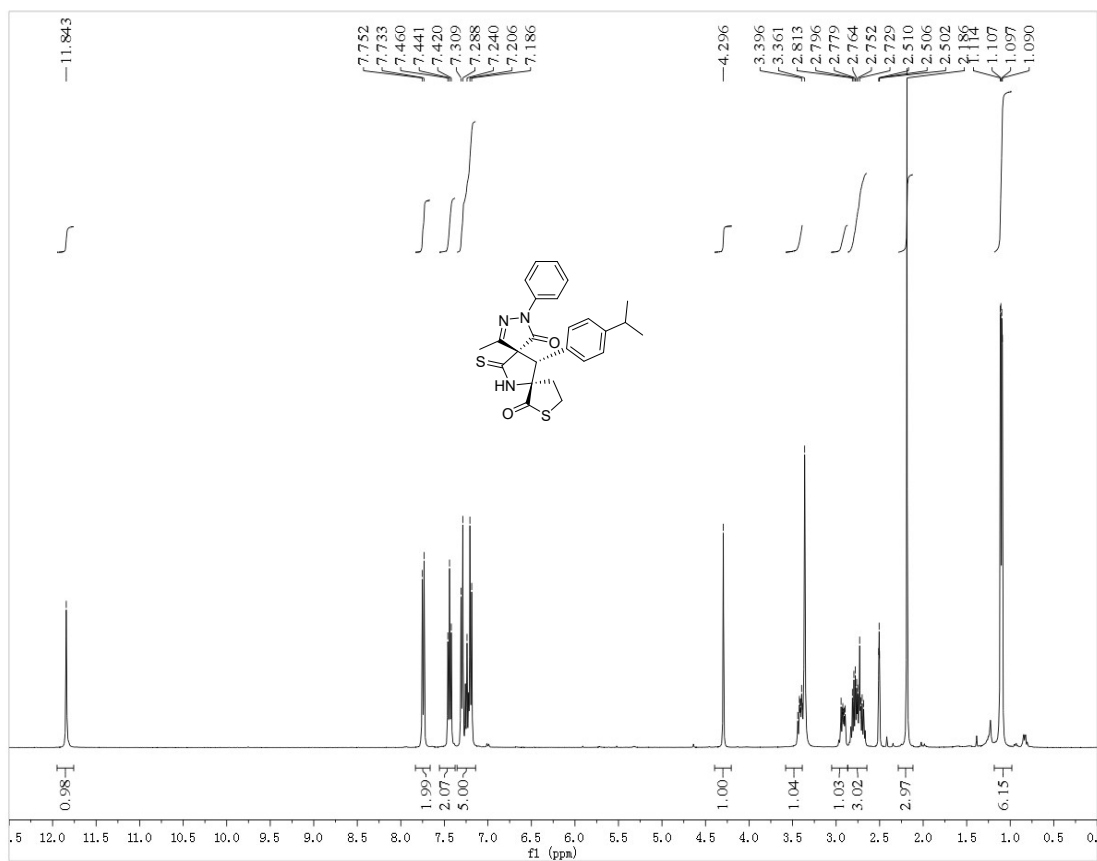
¹H and ¹³C NMR of 3f



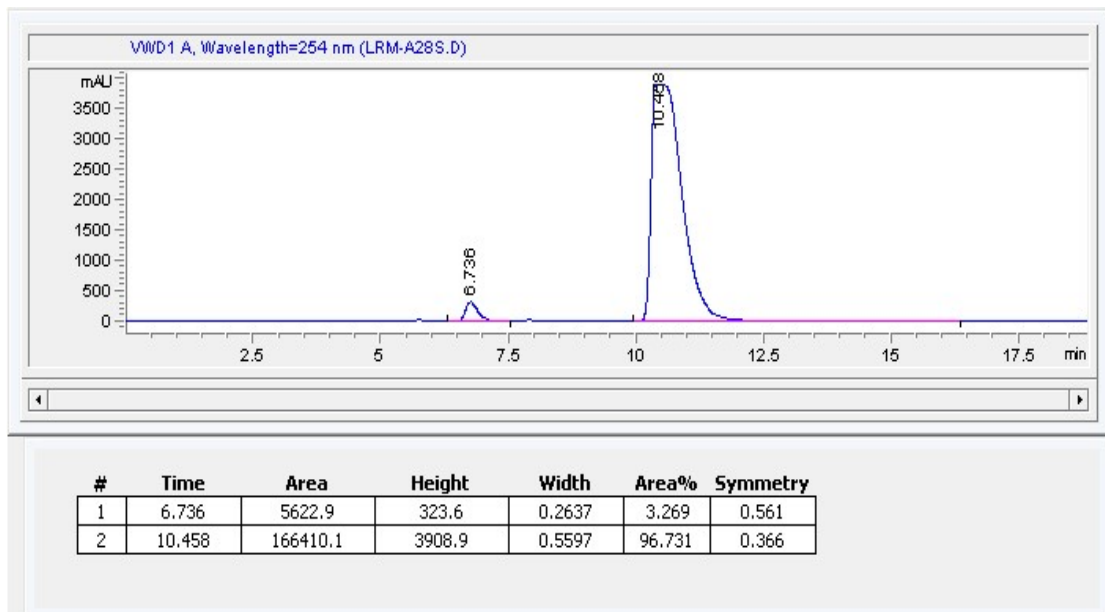
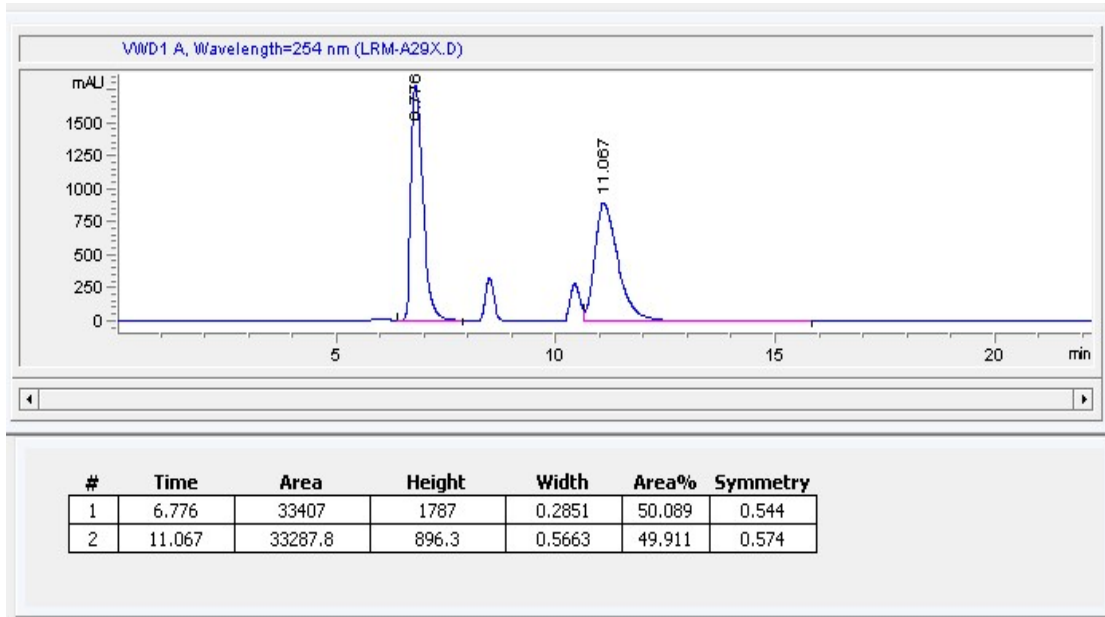
HPLC of 3f



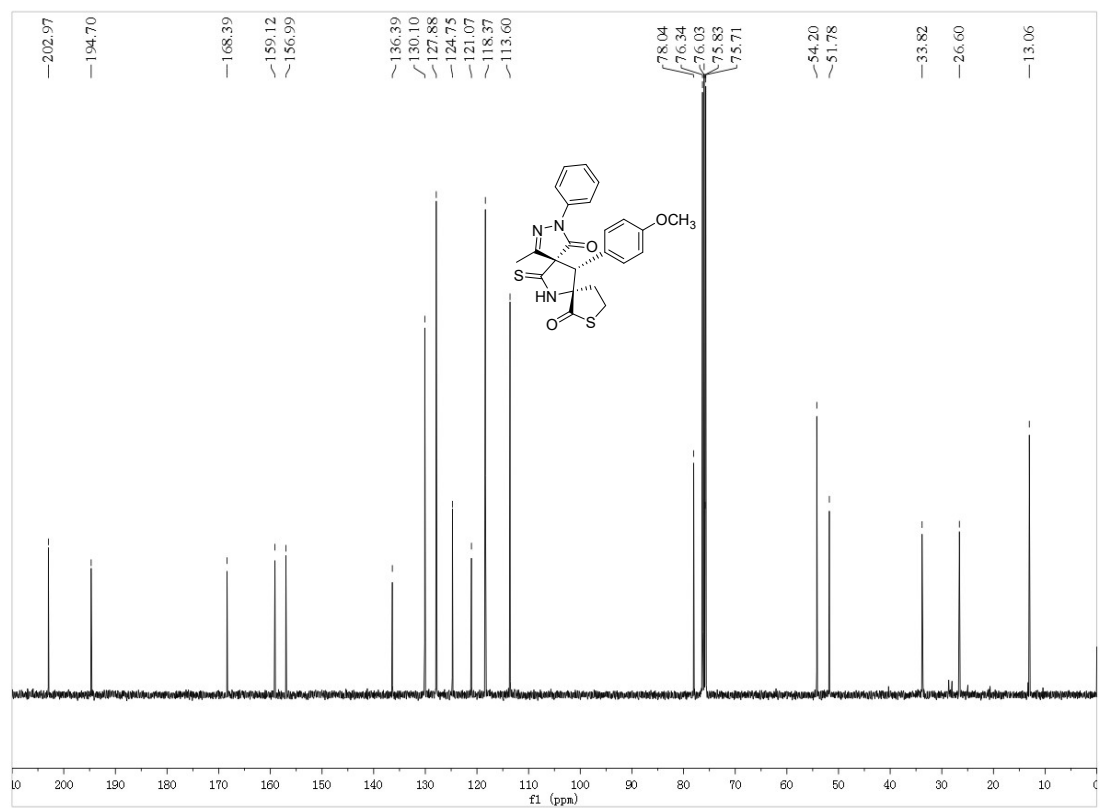
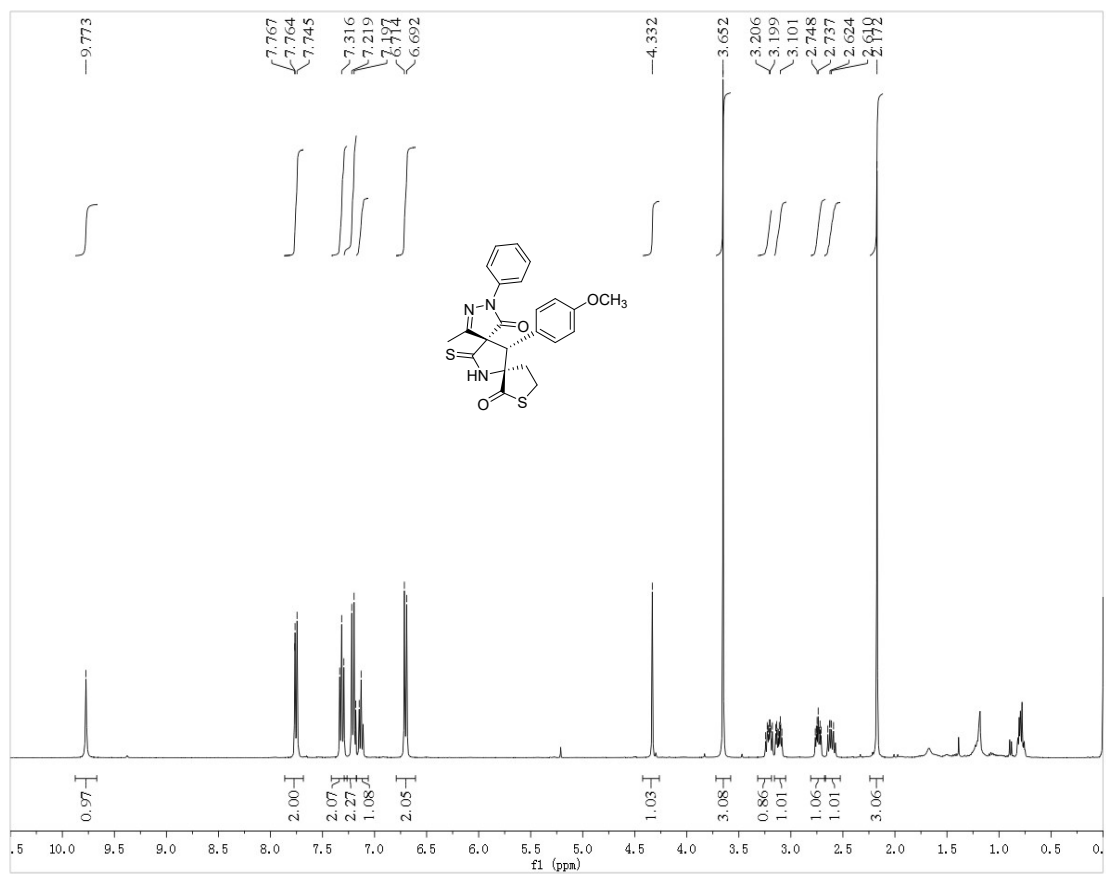
¹H and ¹³C NMR of 3g



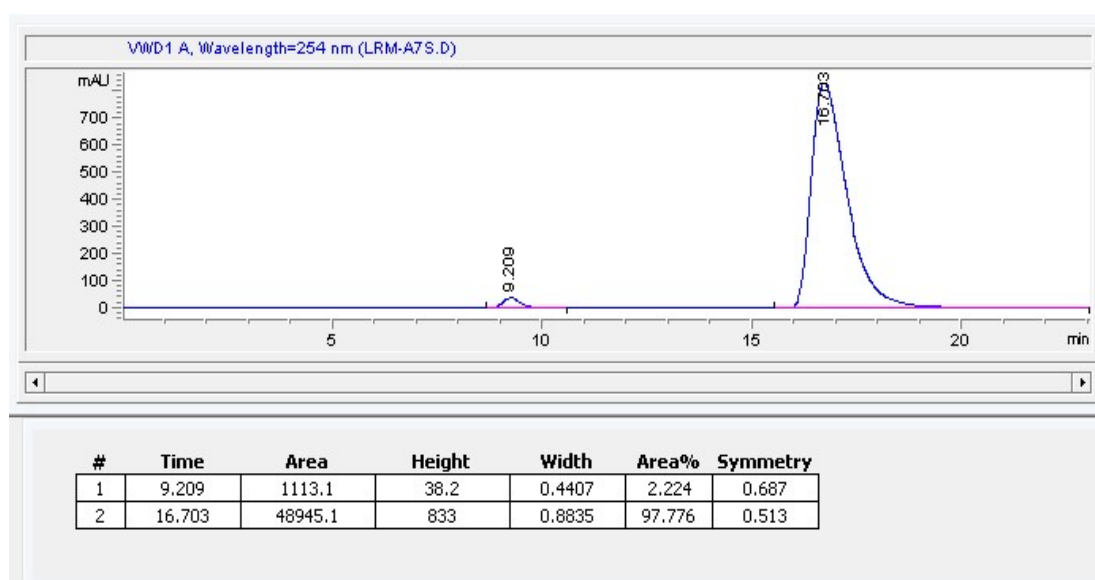
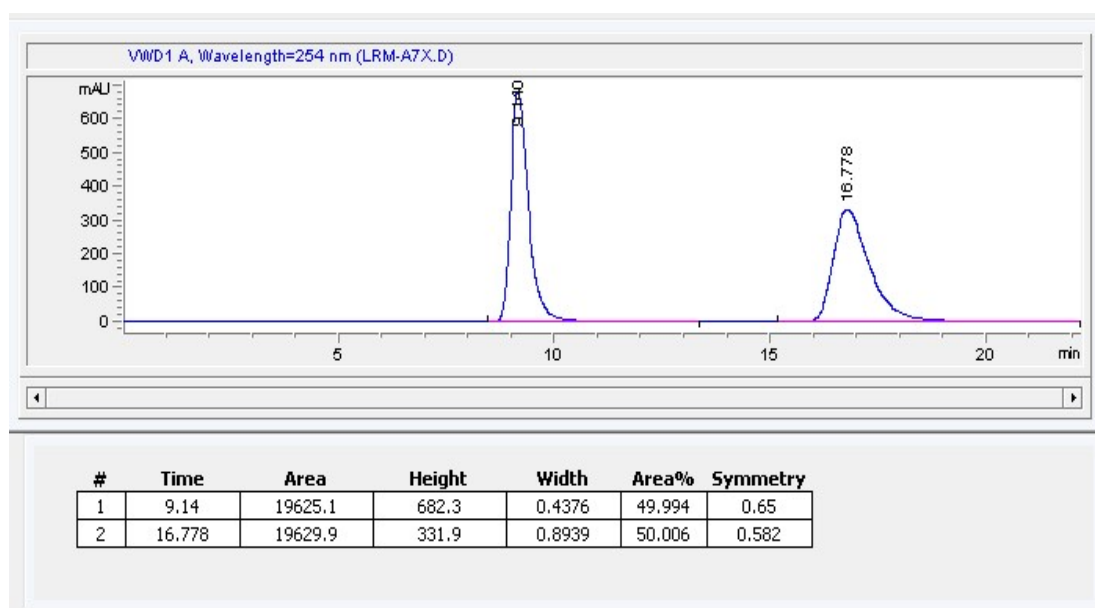
HPLC of 3g



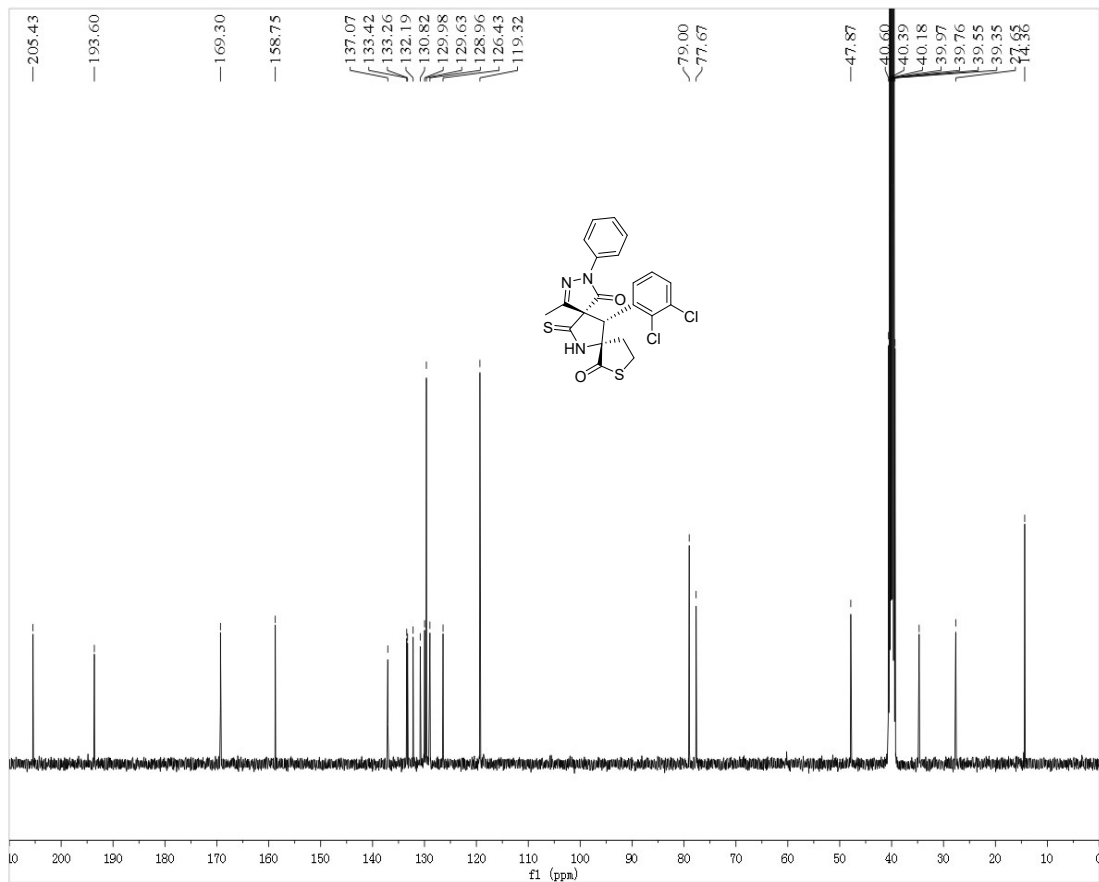
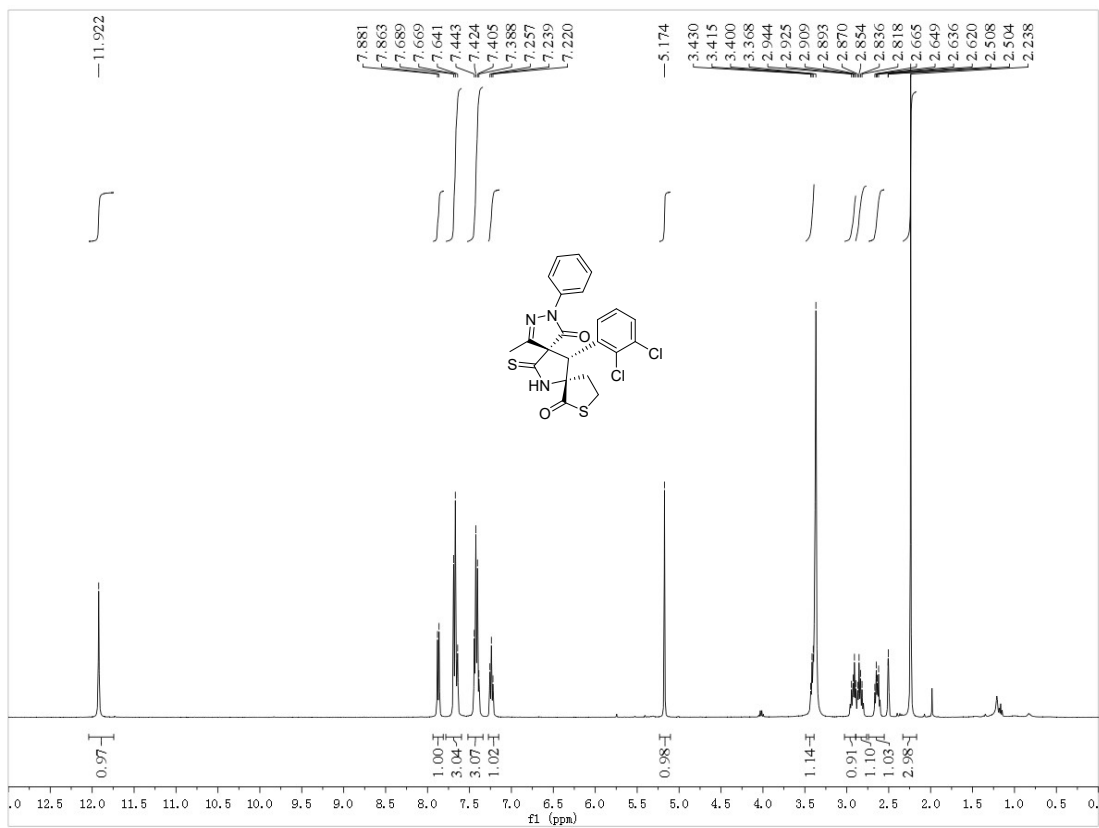
¹H and ¹³C NMR of 3h



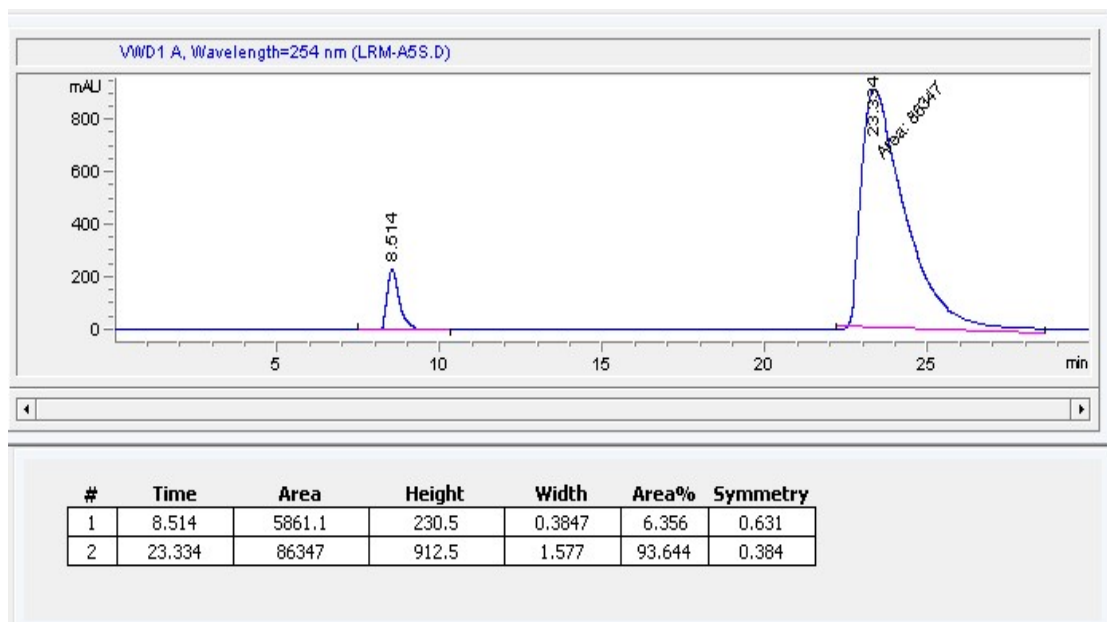
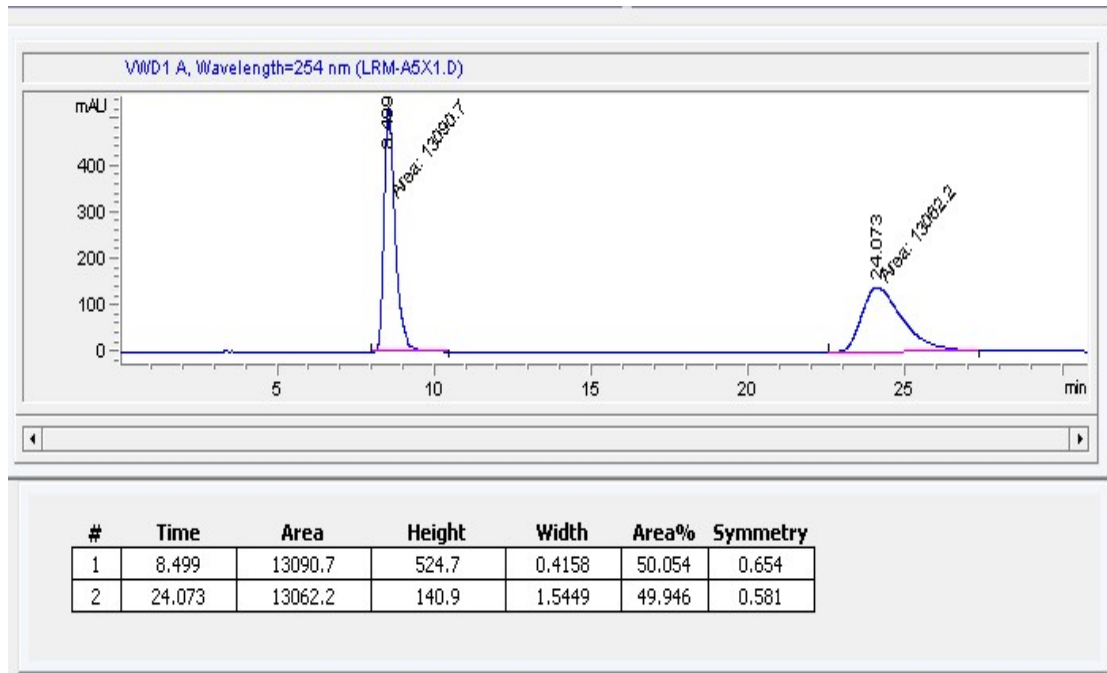
HPLC of 3h



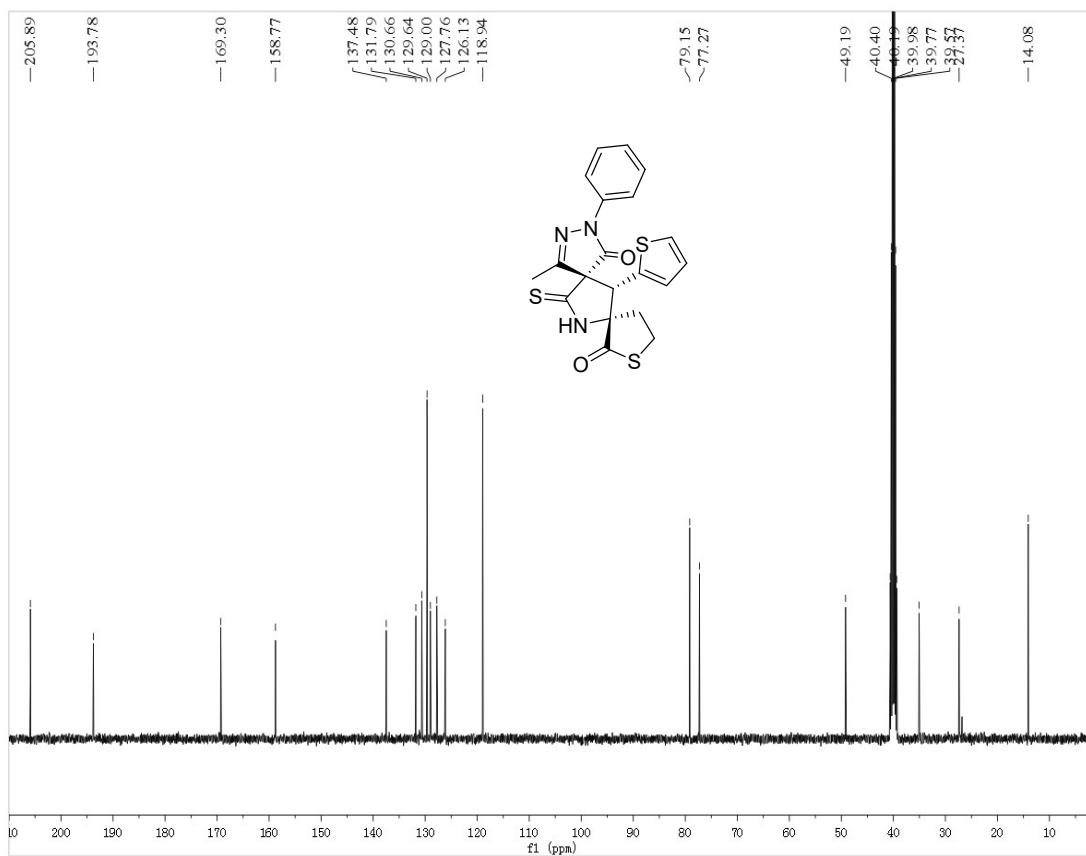
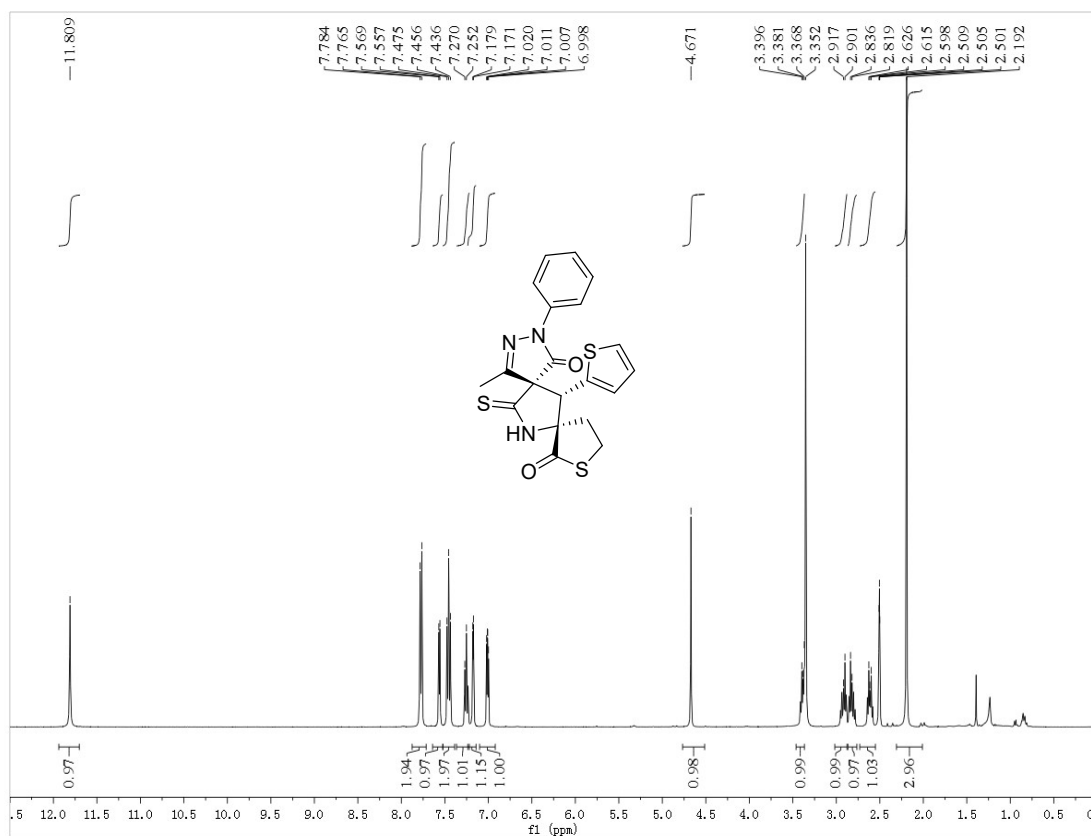
^1H and ^{13}C NMR of 3i



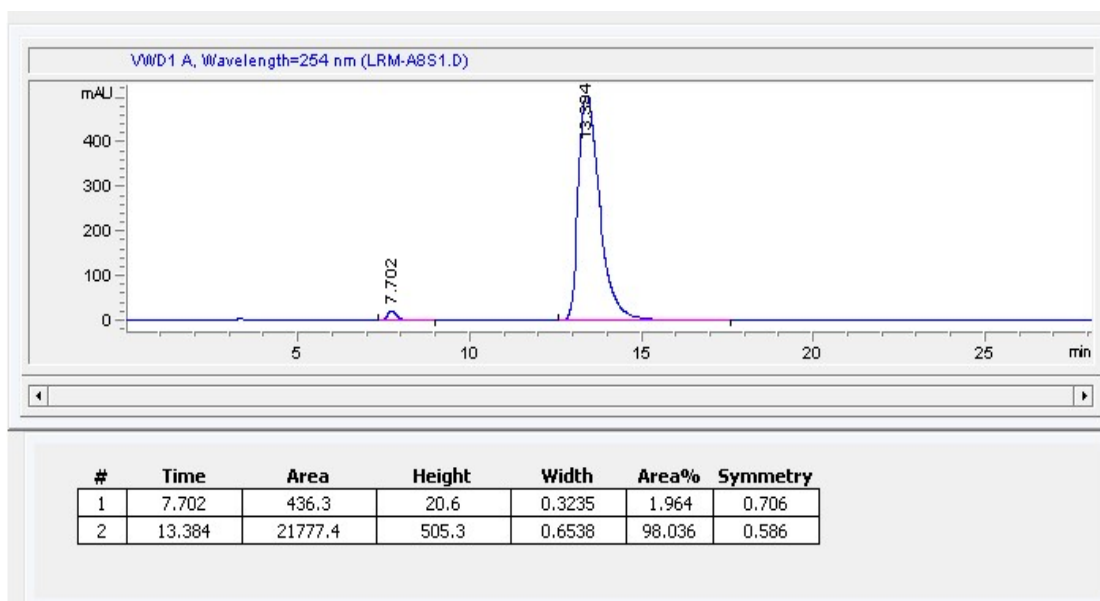
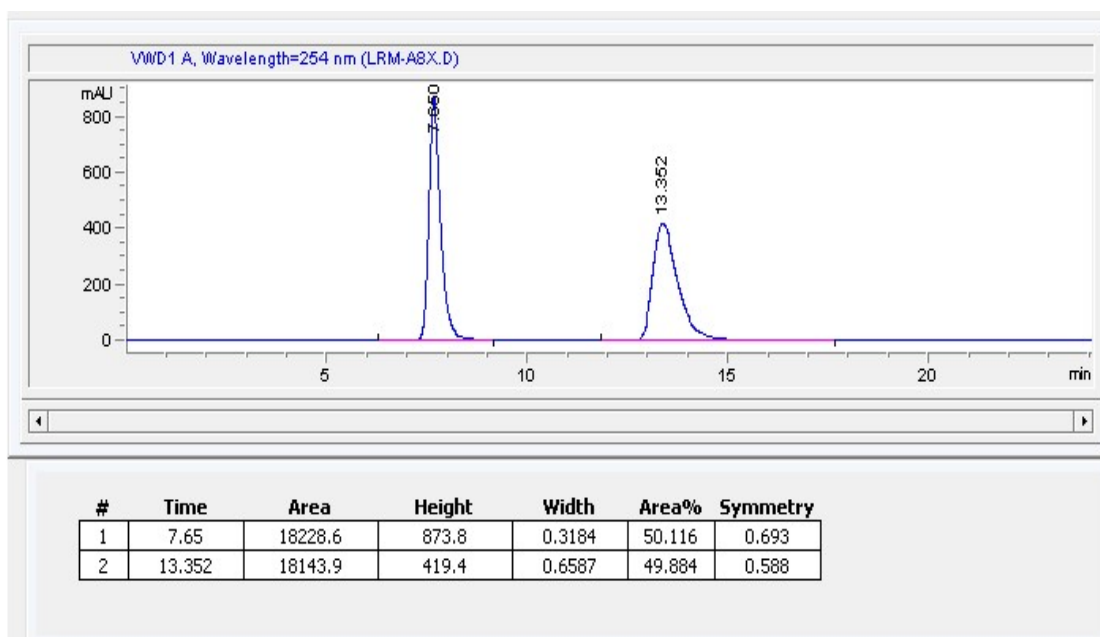
HPLC of 3i



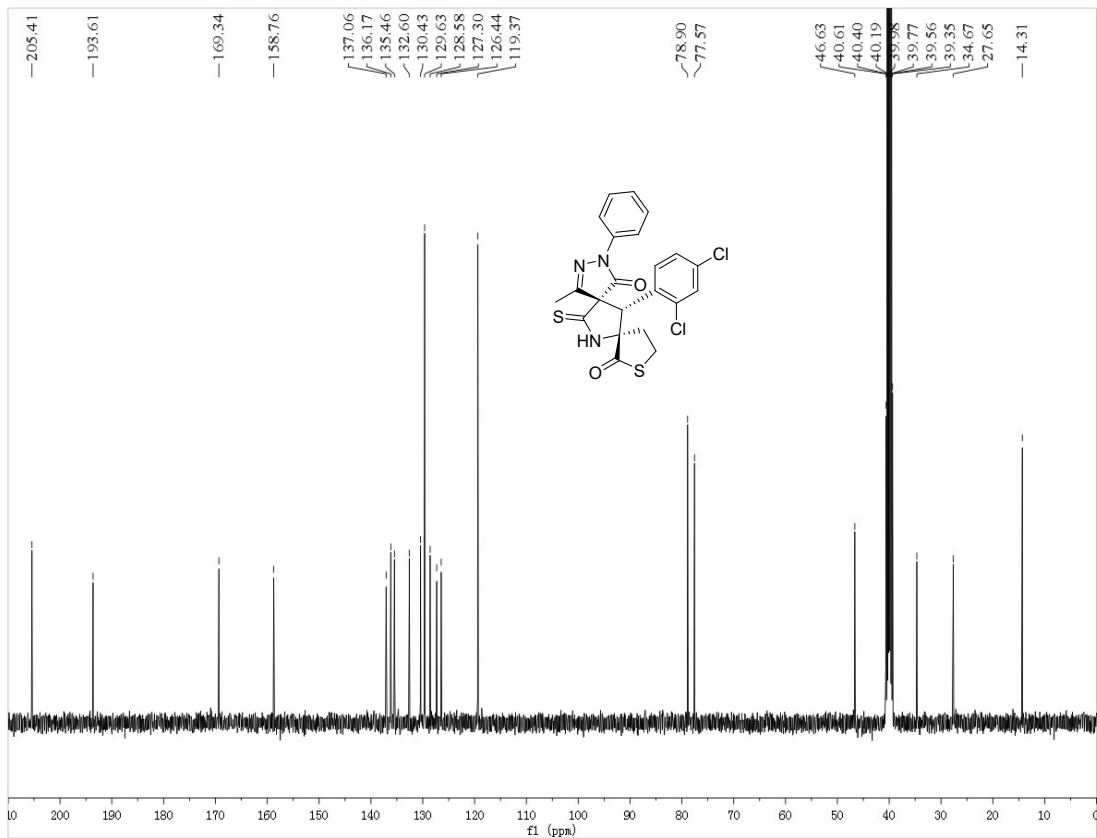
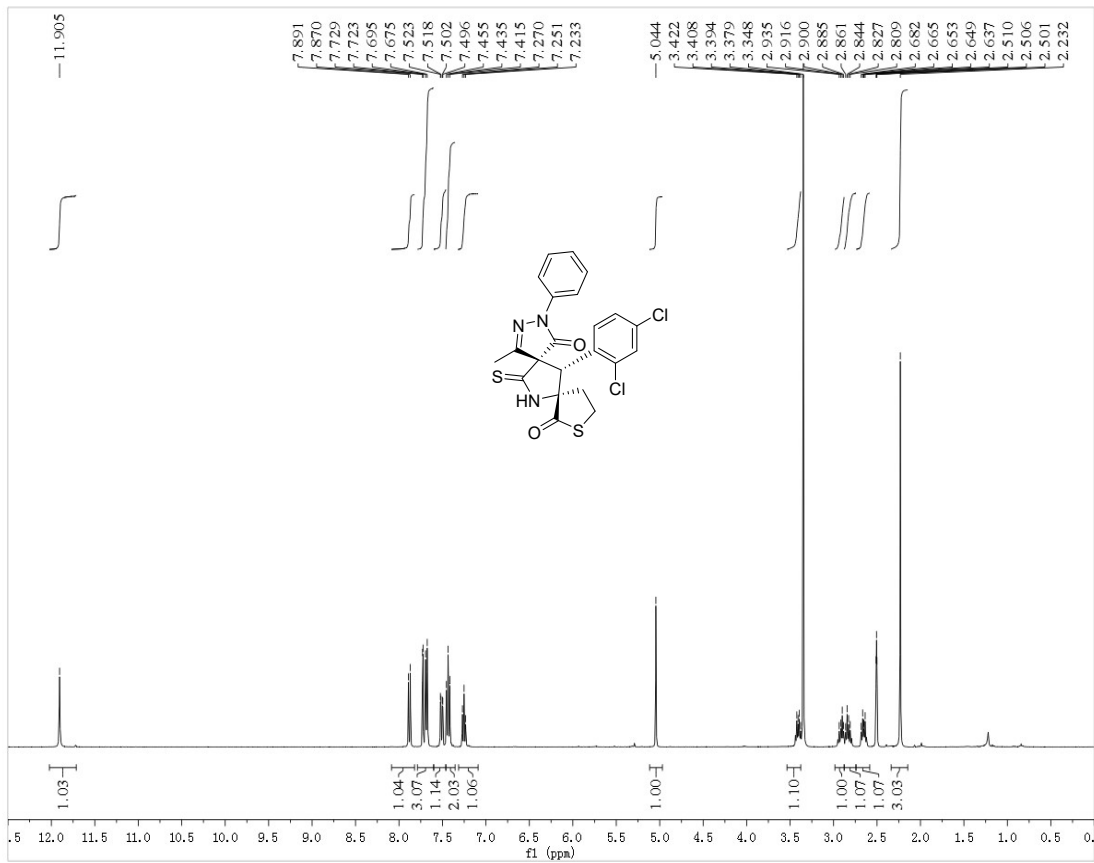
¹H and ¹³C NMR of 3j



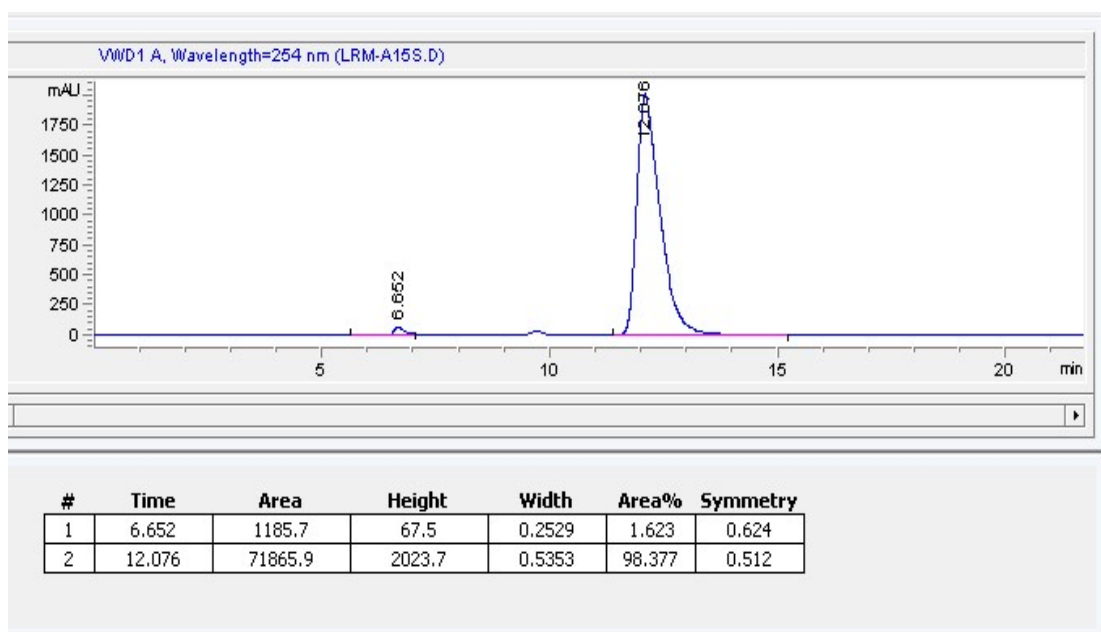
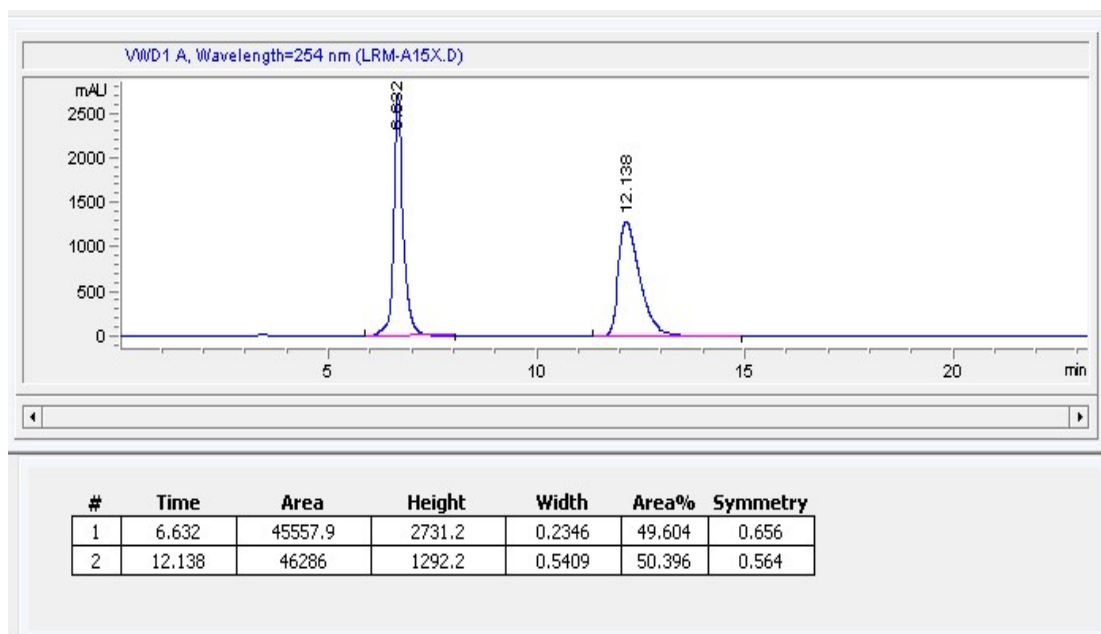
HPLC of 3j



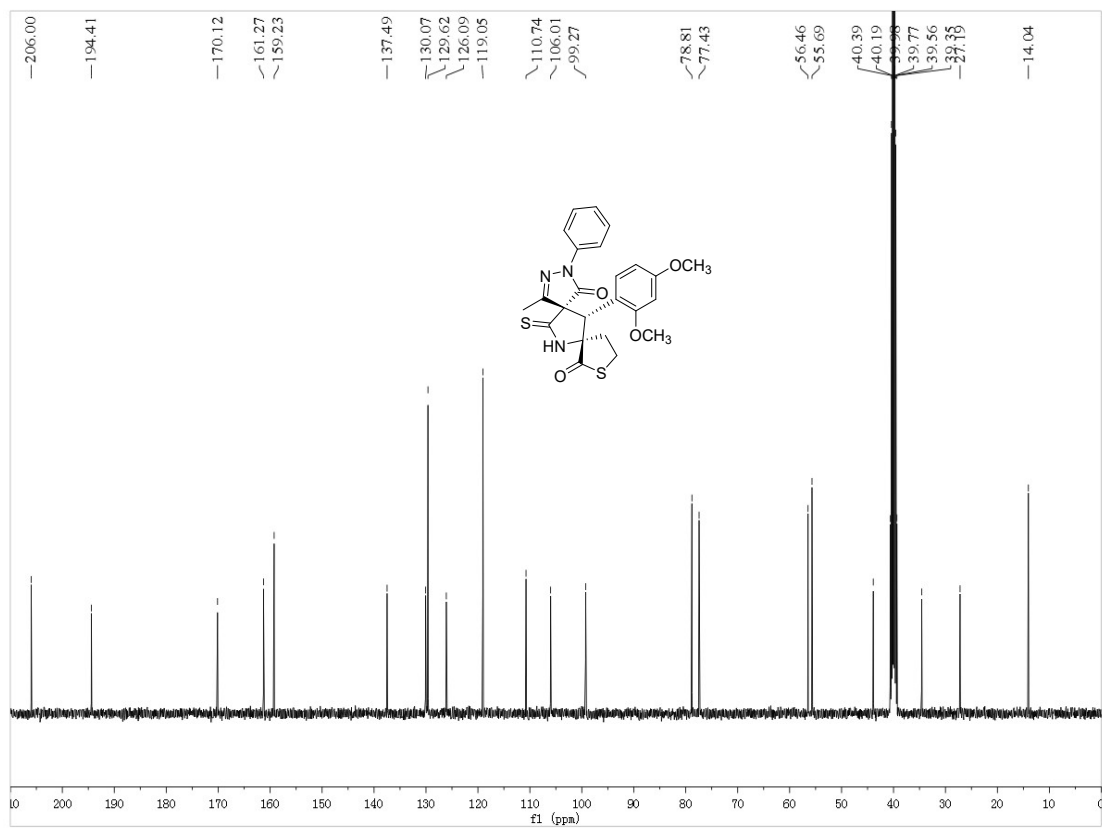
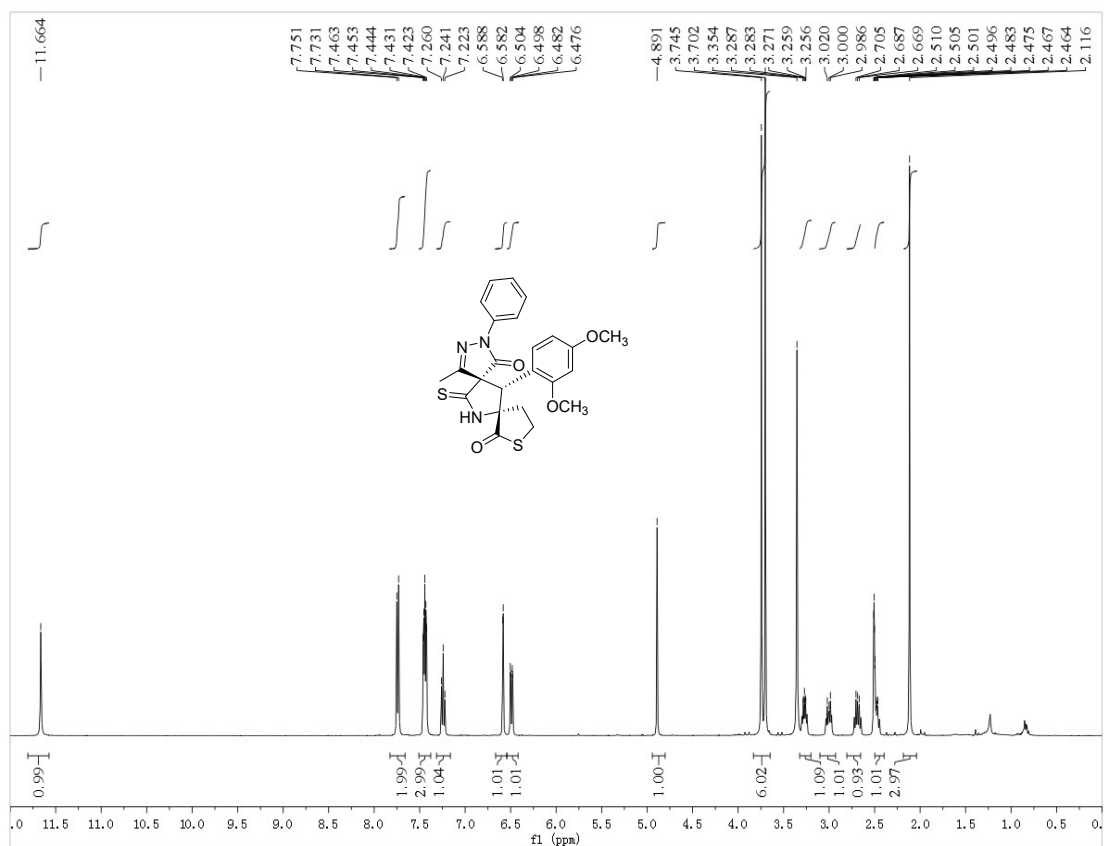
¹H and ¹³C NMR of 3k



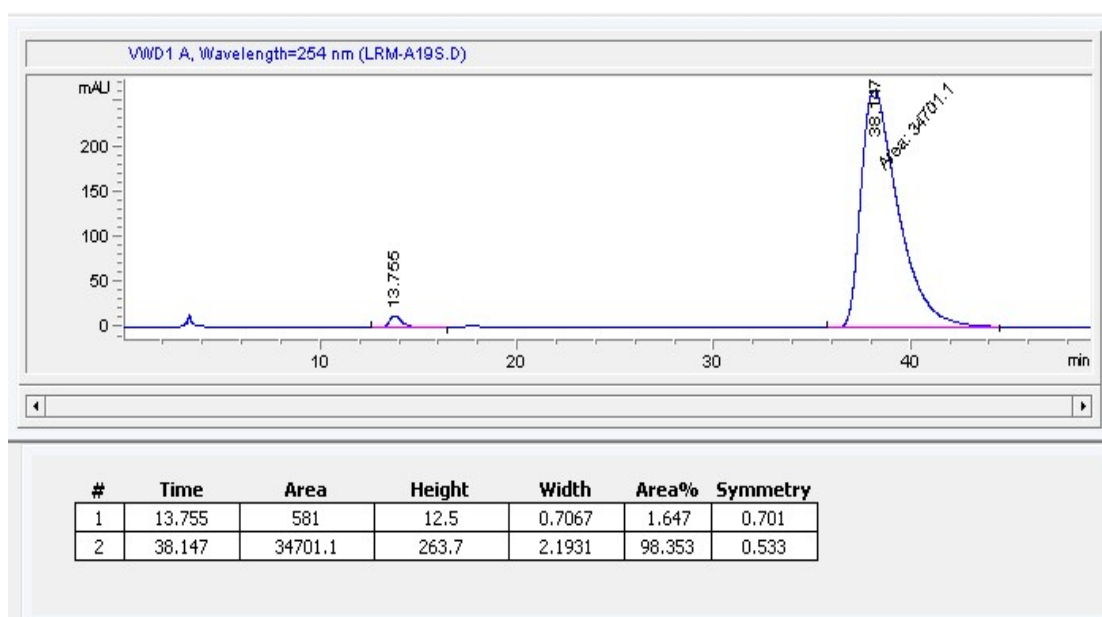
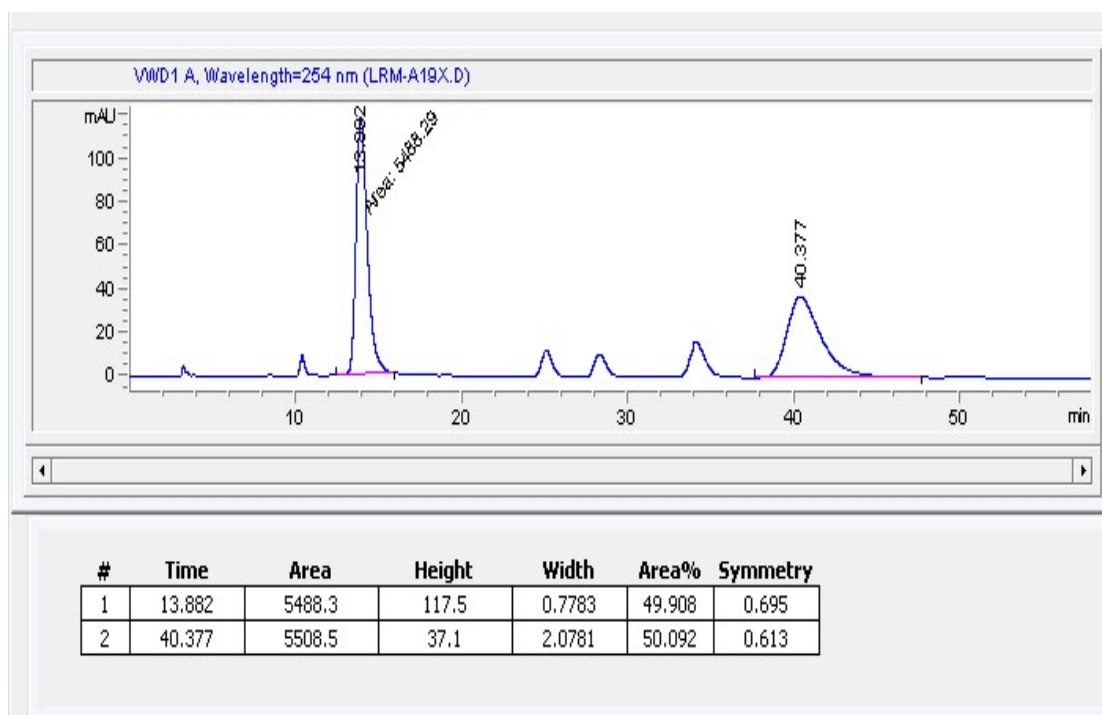
HPLC of 3k



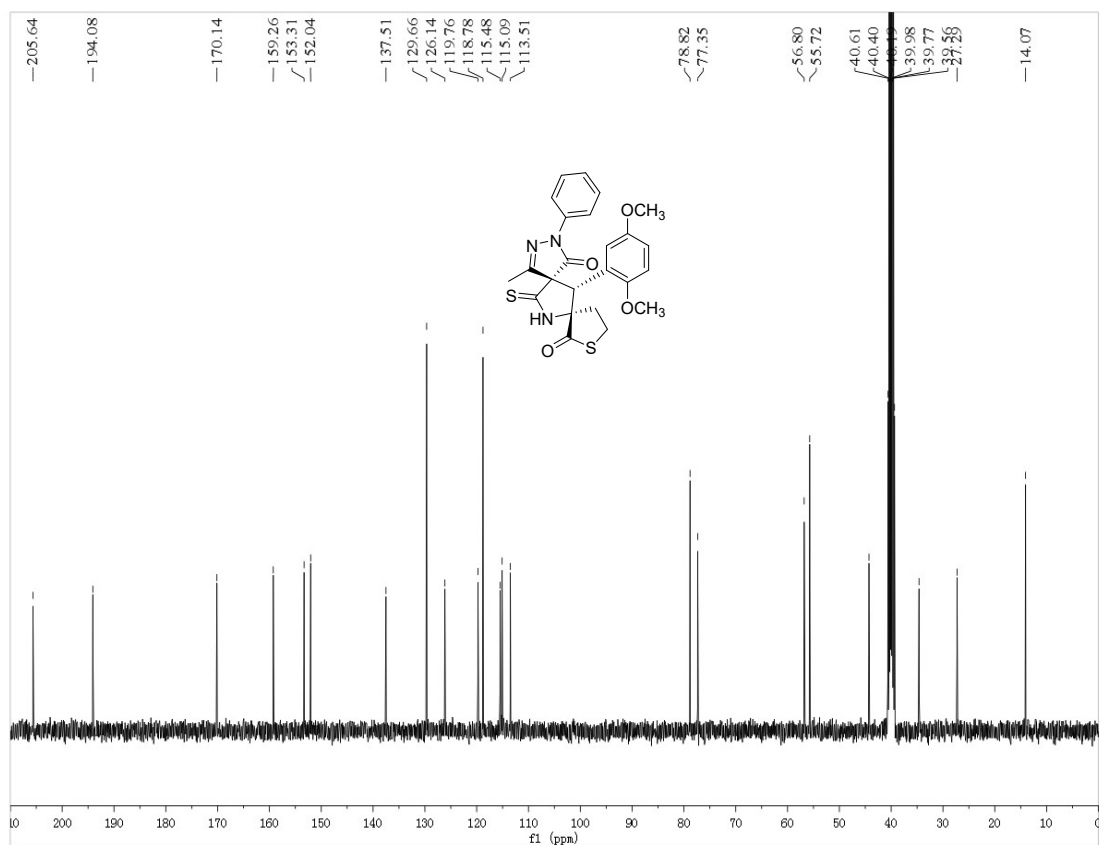
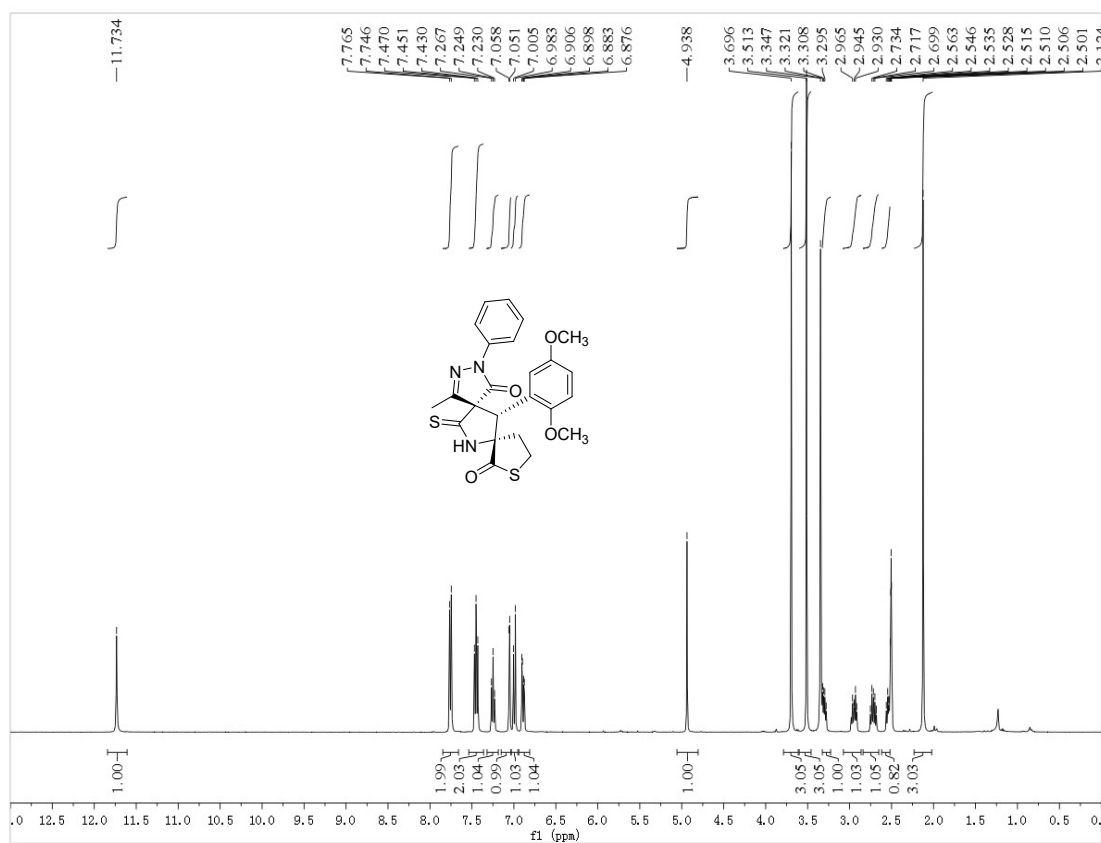
^1H and ^{13}C NMR of 3l



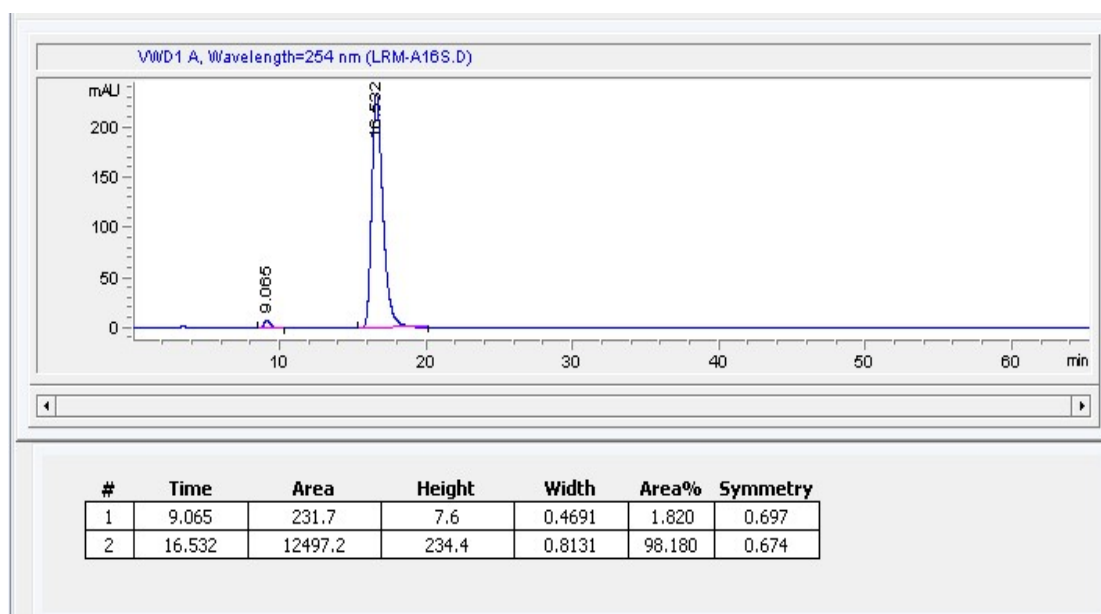
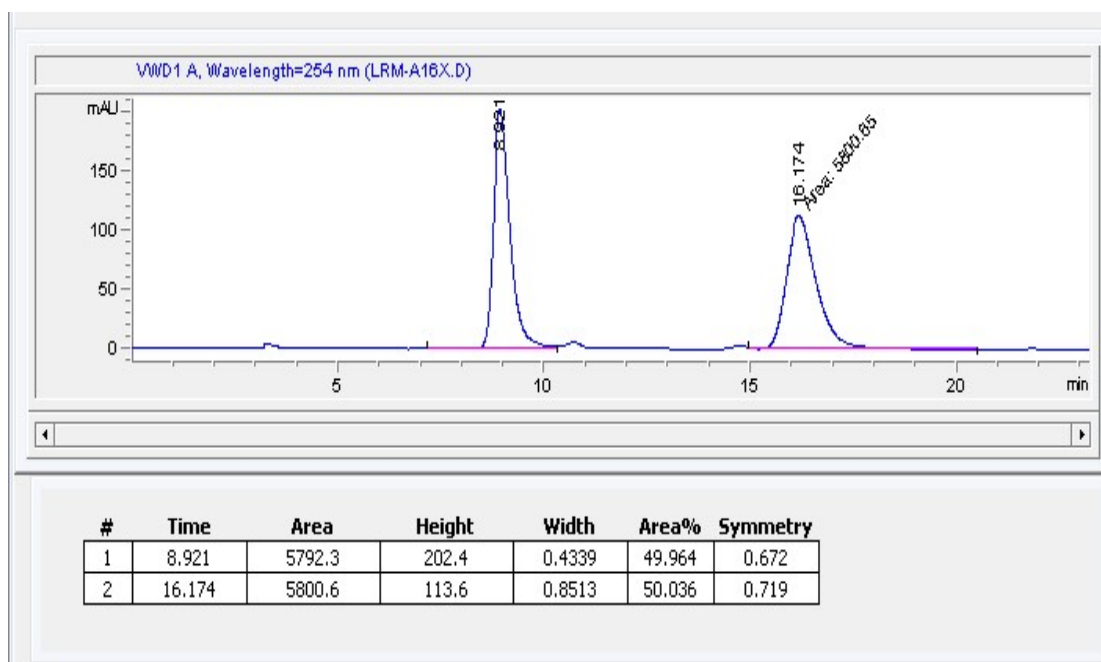
HPLC of 31



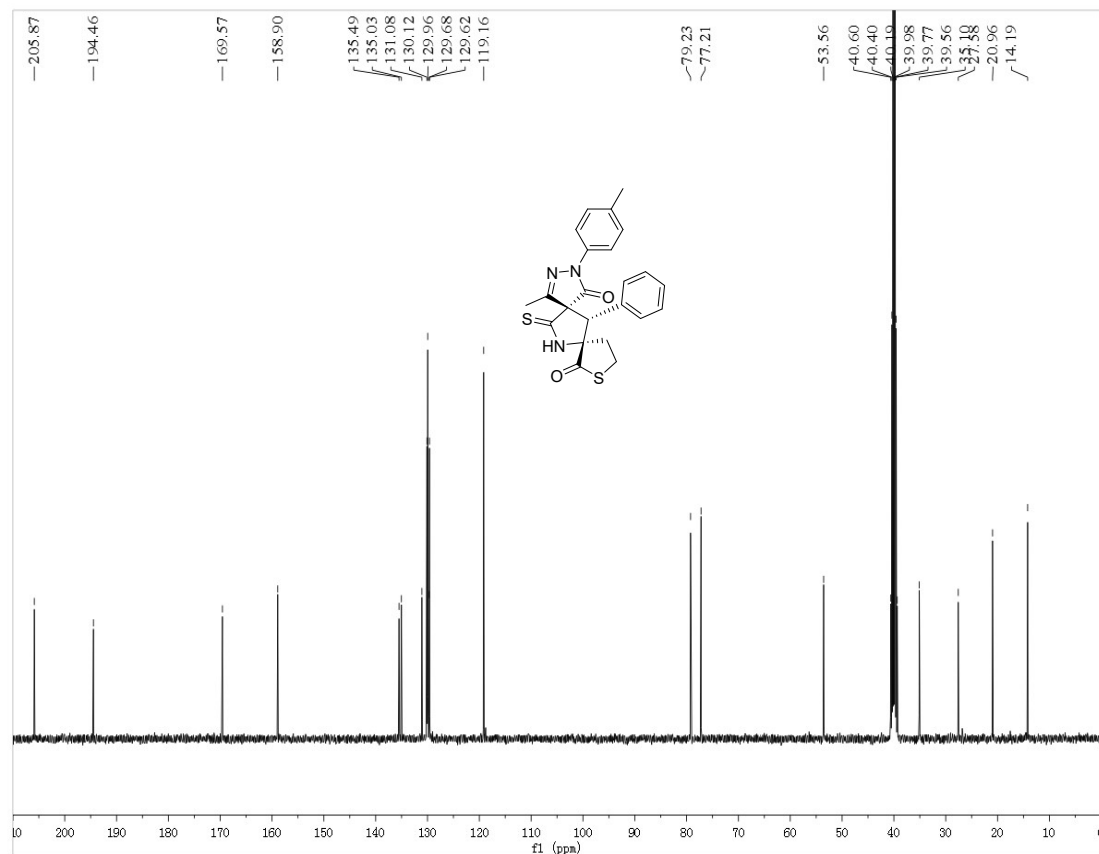
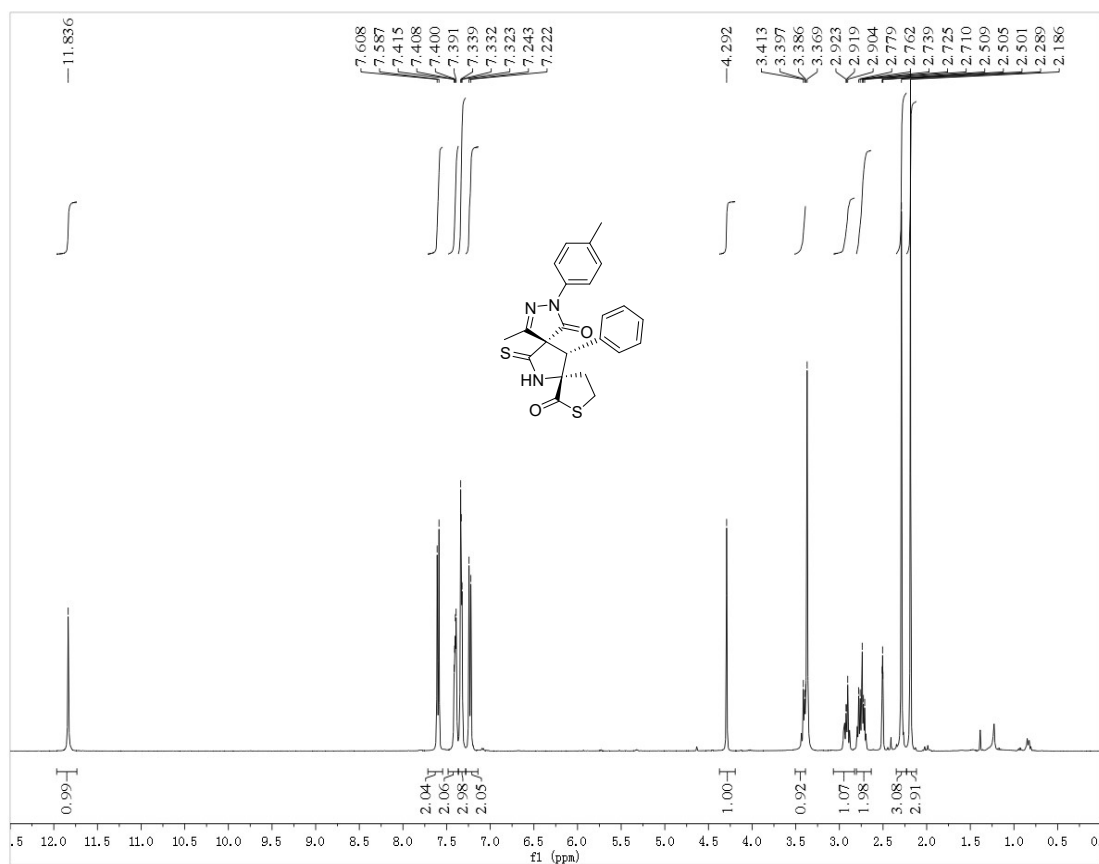
¹H and ¹³C NMR of 3m



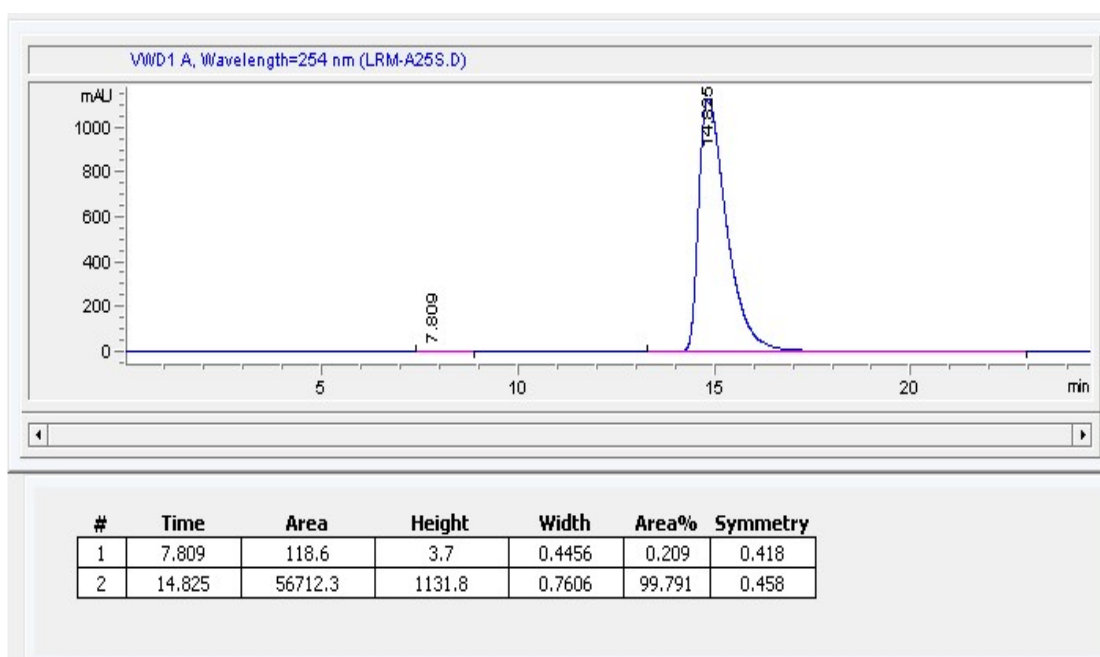
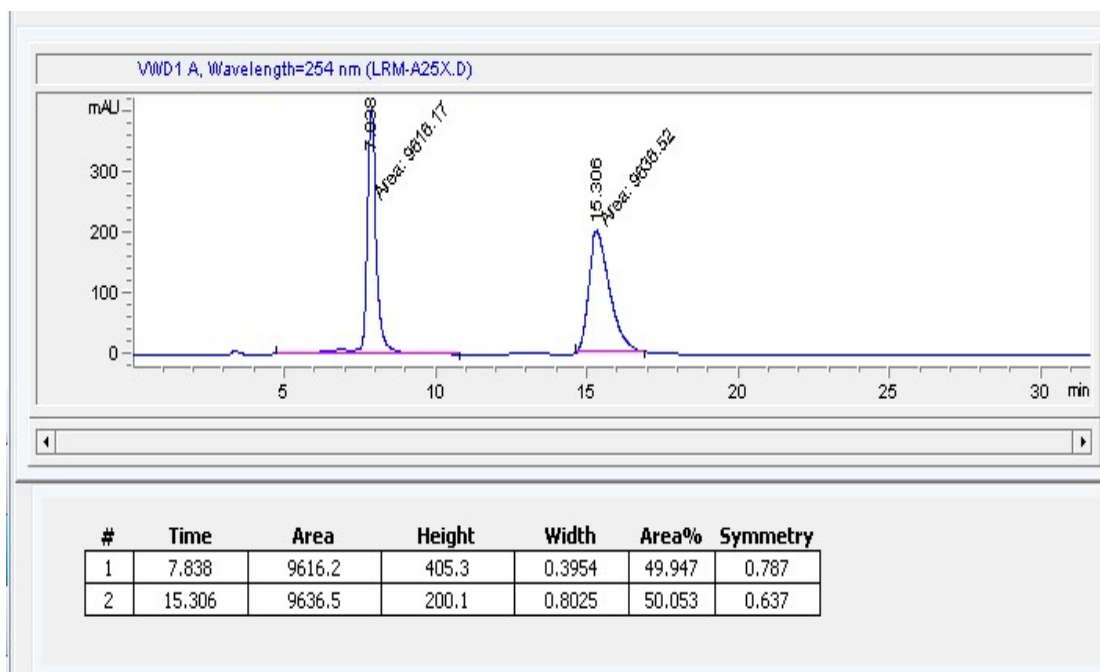
HPLC of 3m



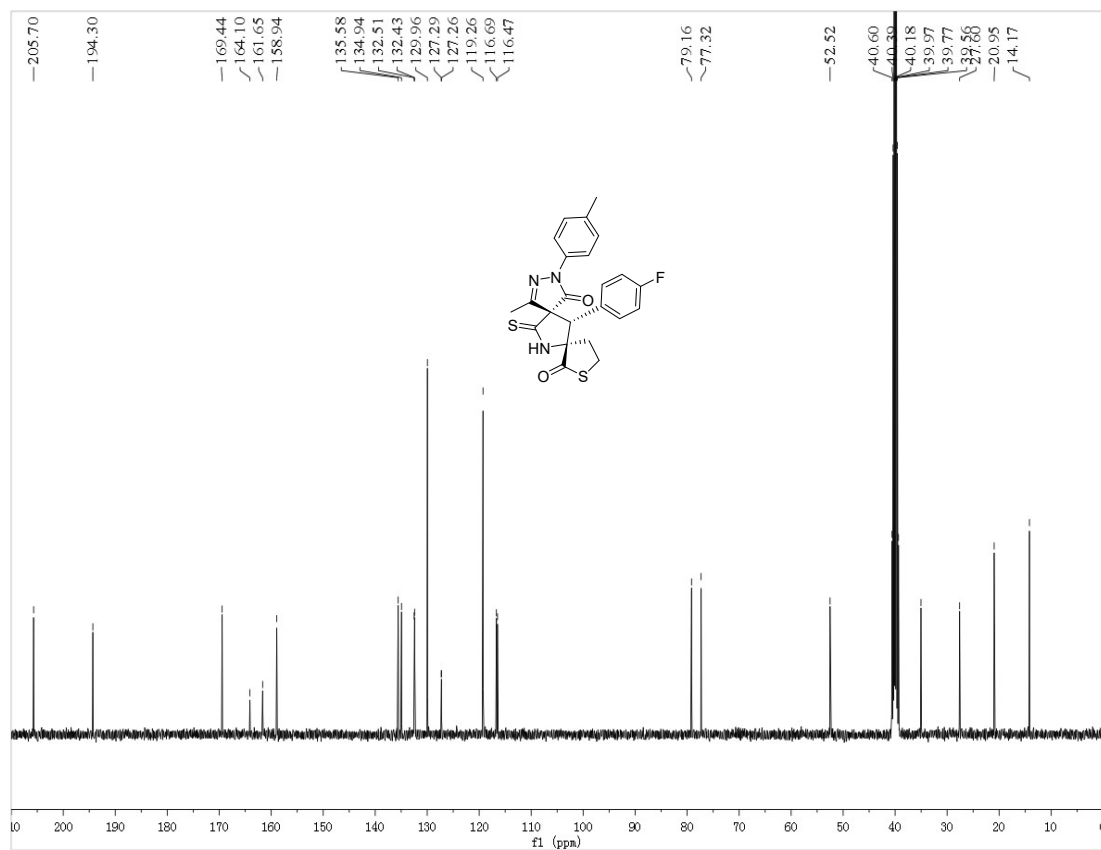
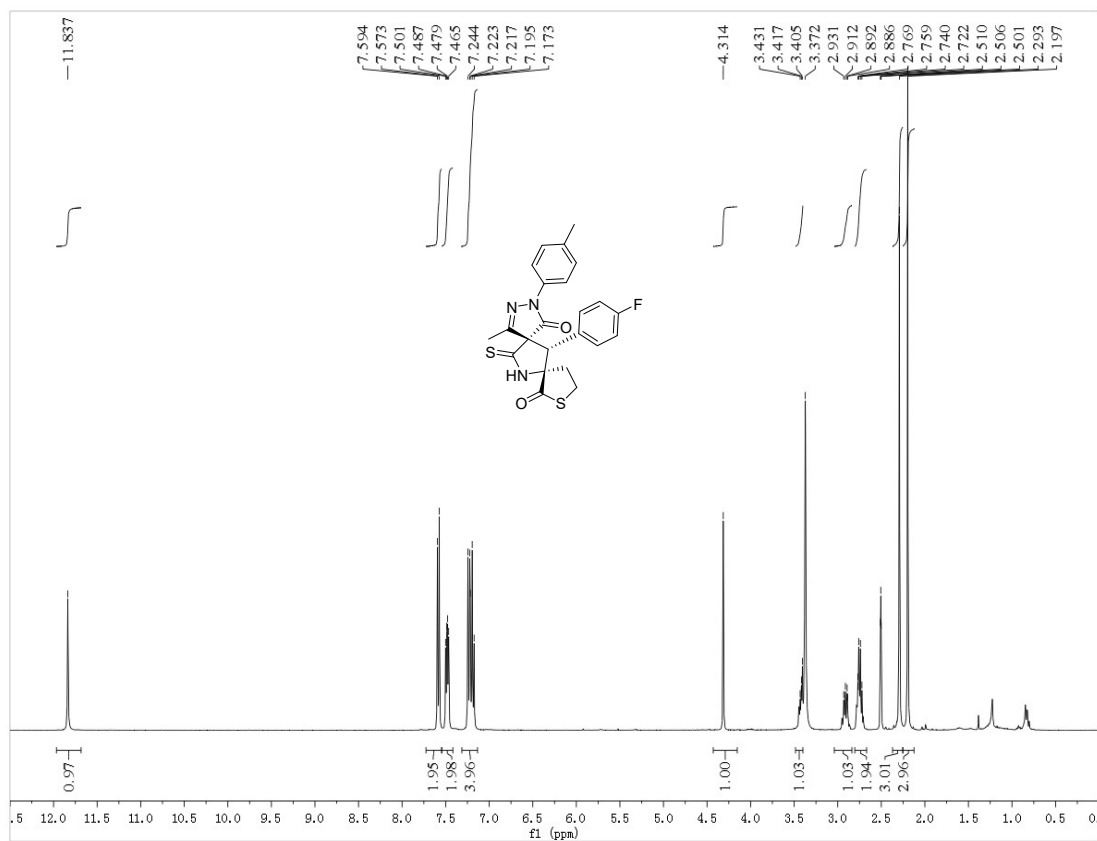
¹H and ¹³C NMR of 3n



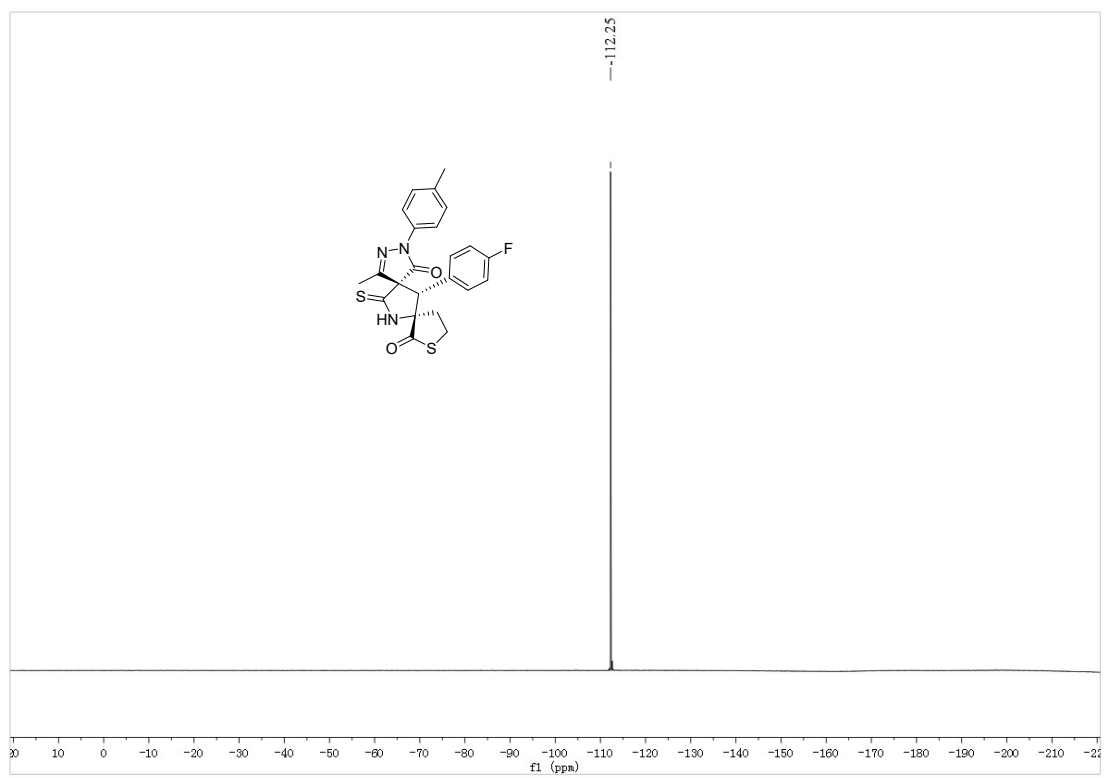
HPLC of 3n



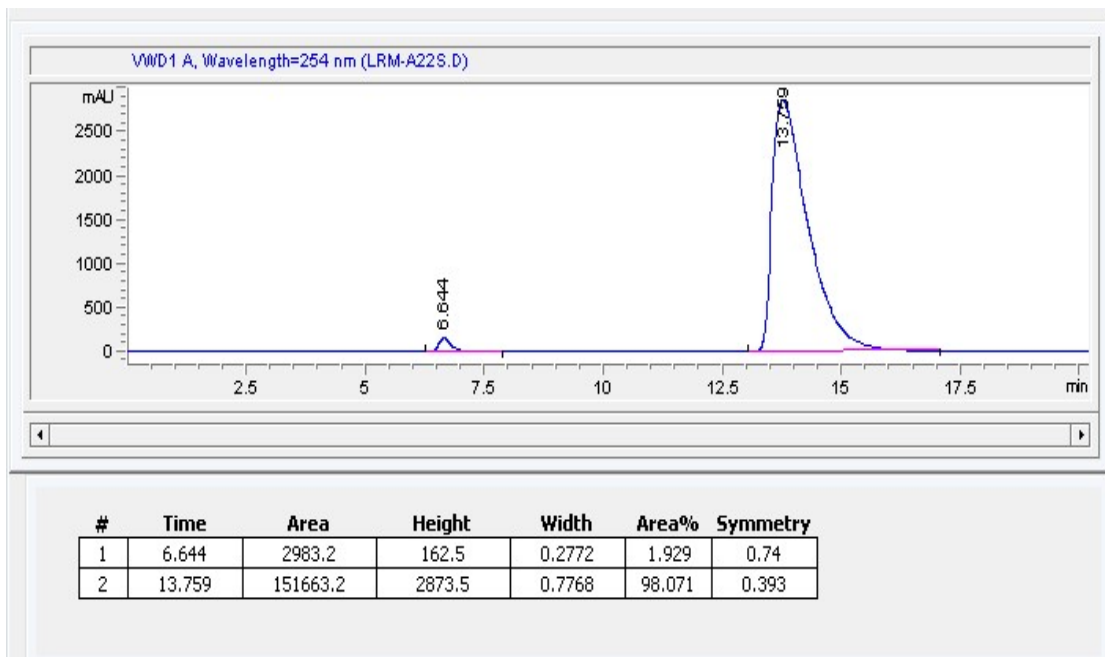
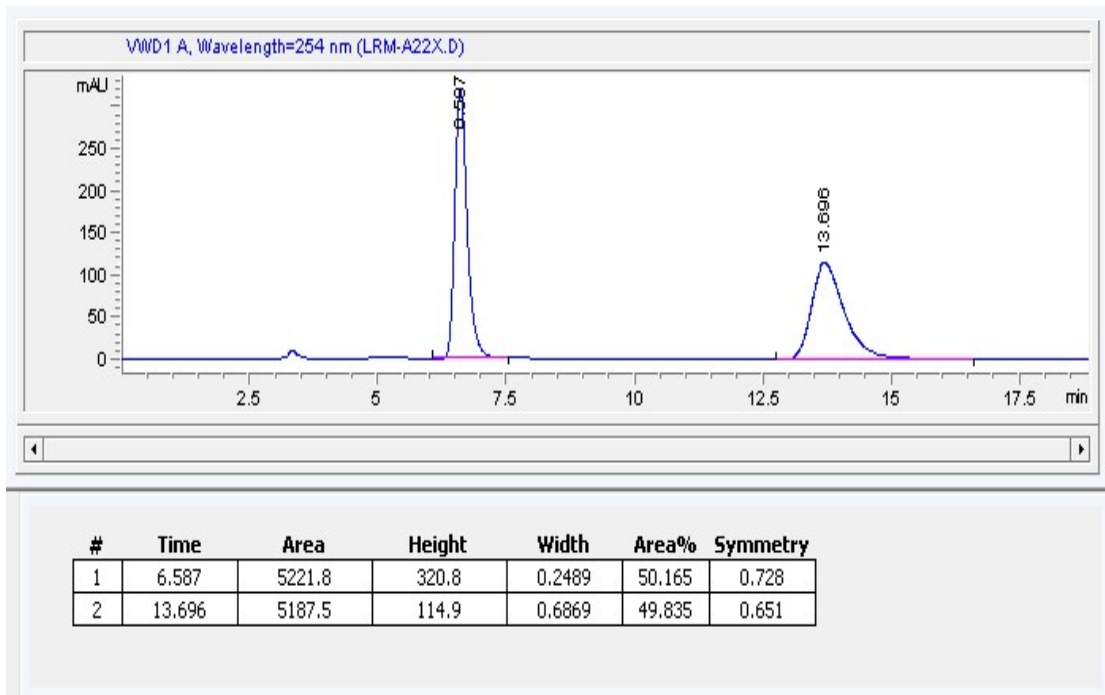
¹H and ¹³C NMR of 3o



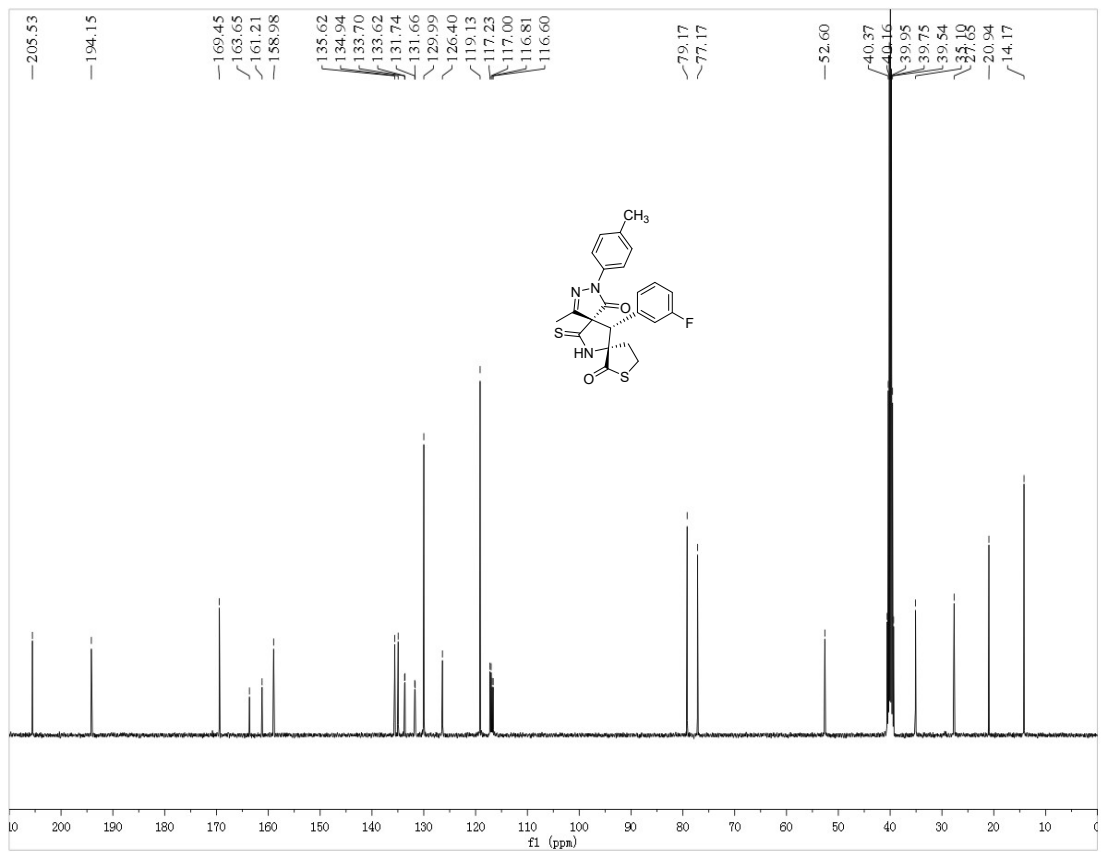
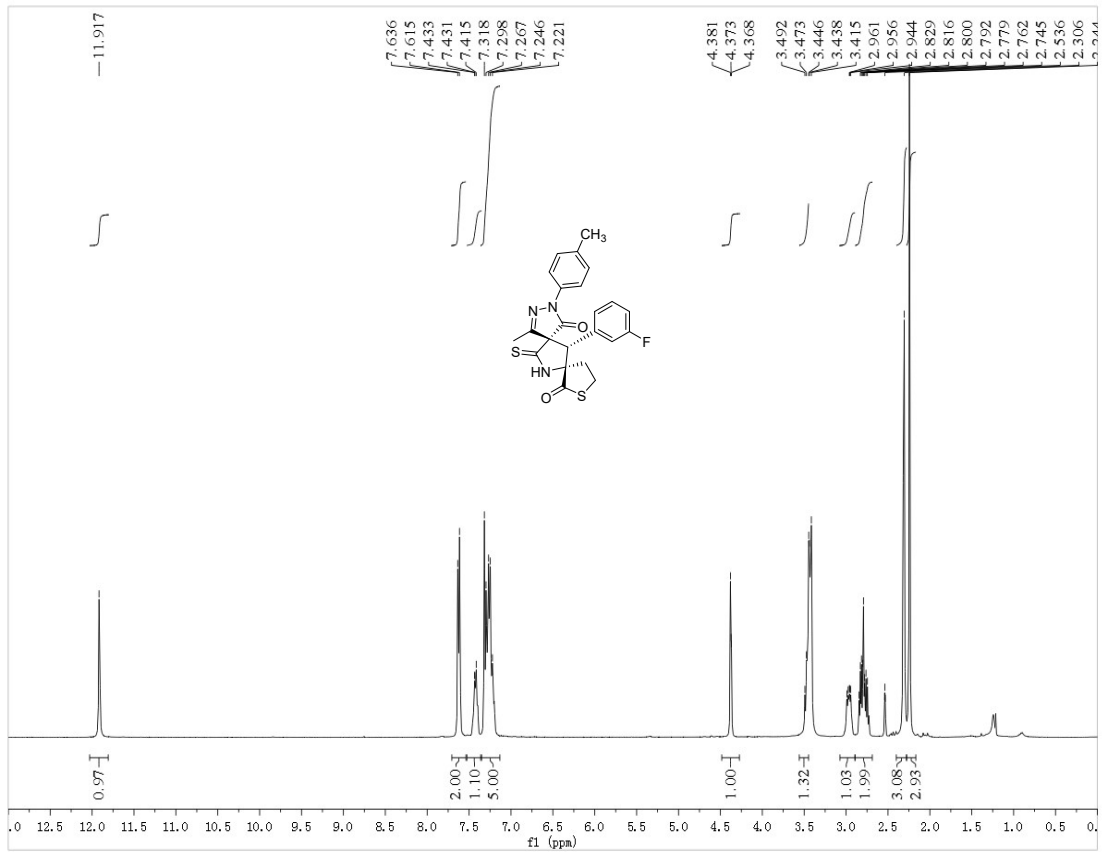
¹⁹F NMR of 3o



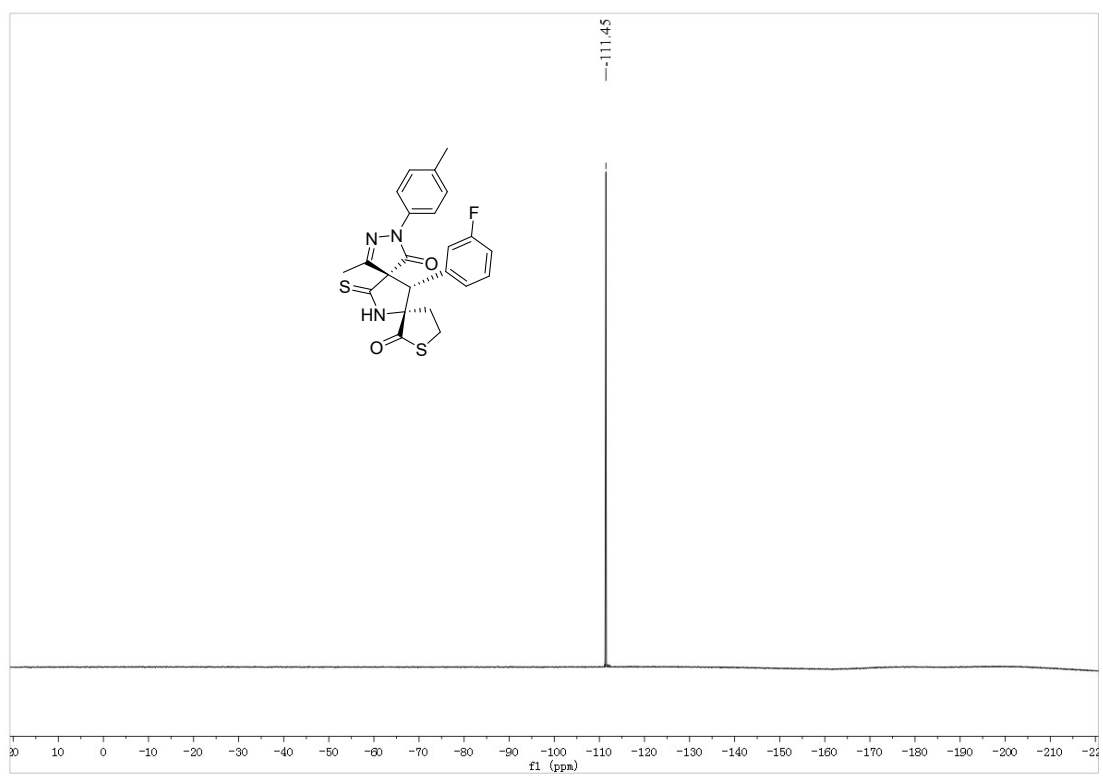
HPLC of 3o



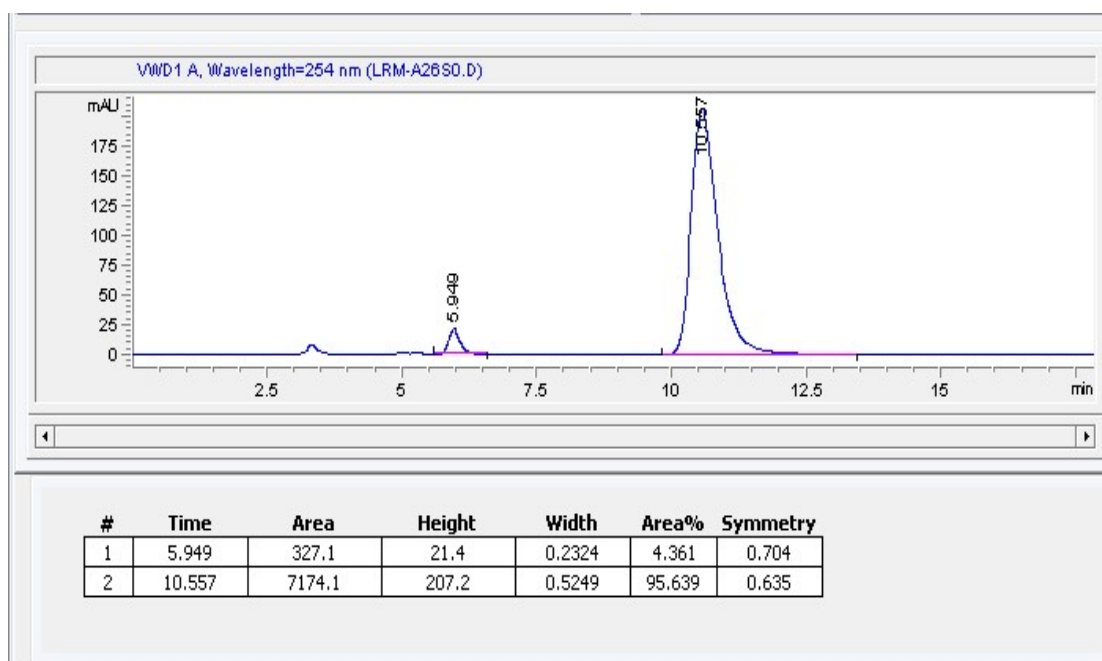
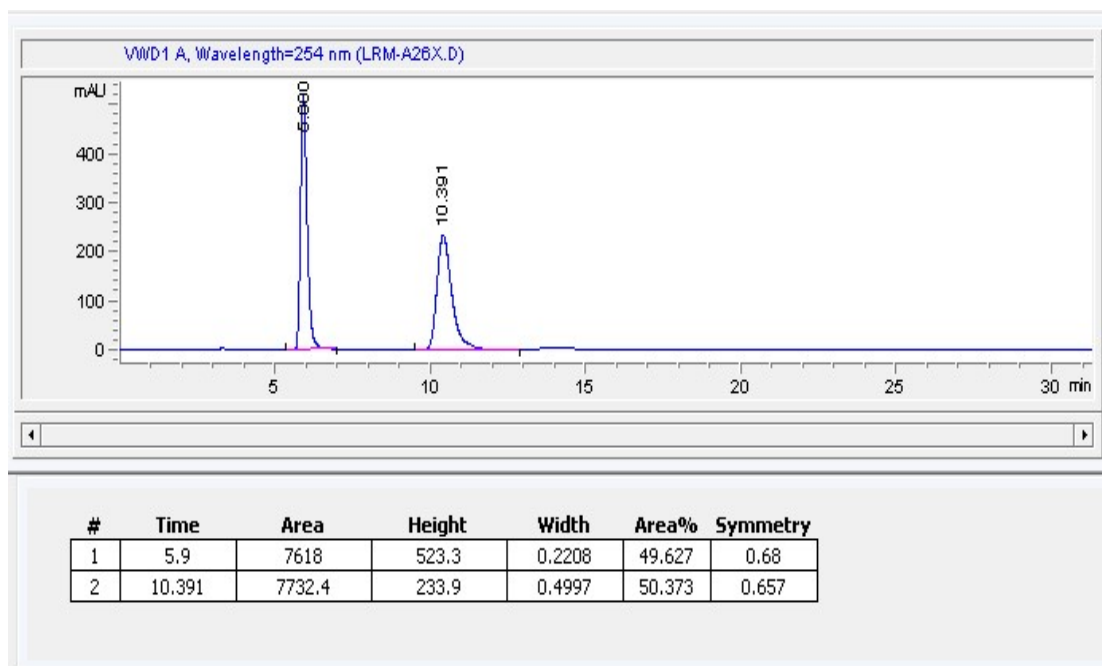
¹H and ¹³C NMR of 3p



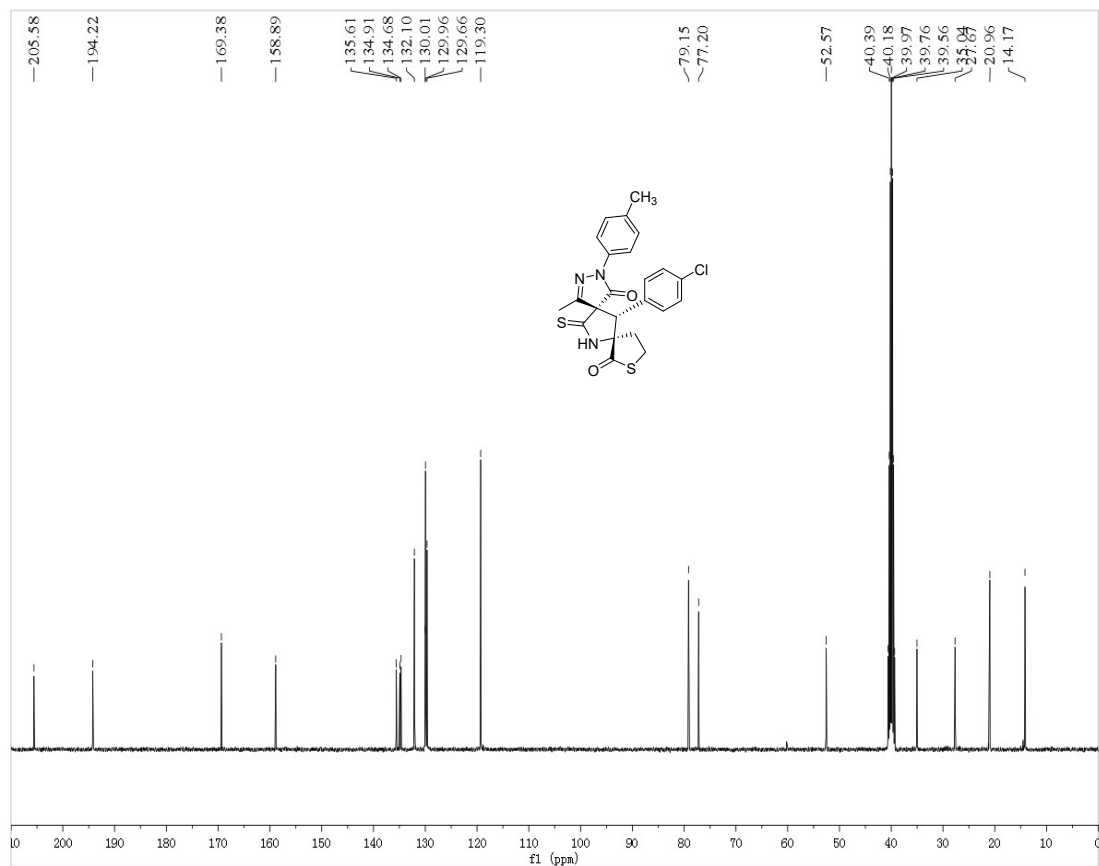
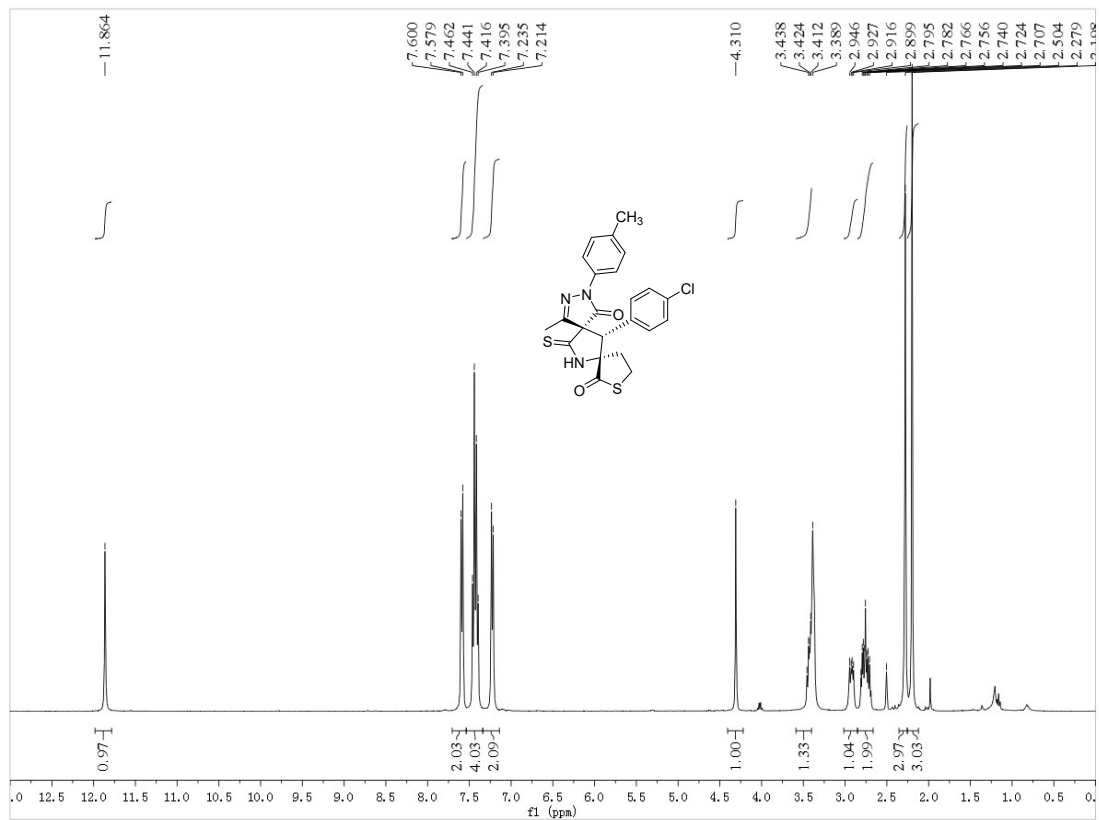
¹⁹F NMR of 3p



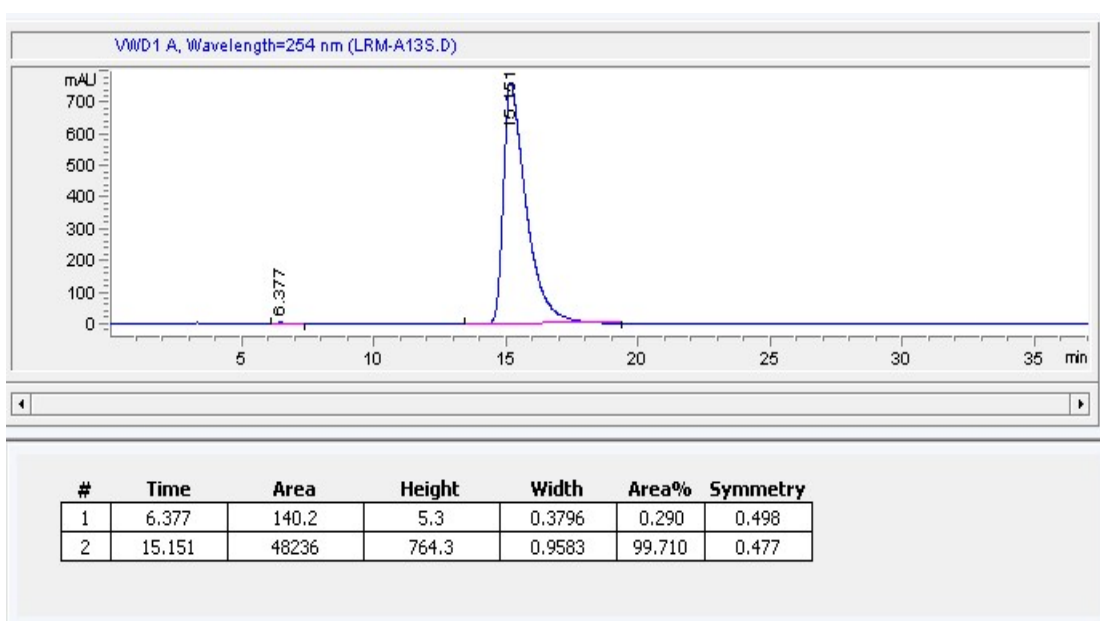
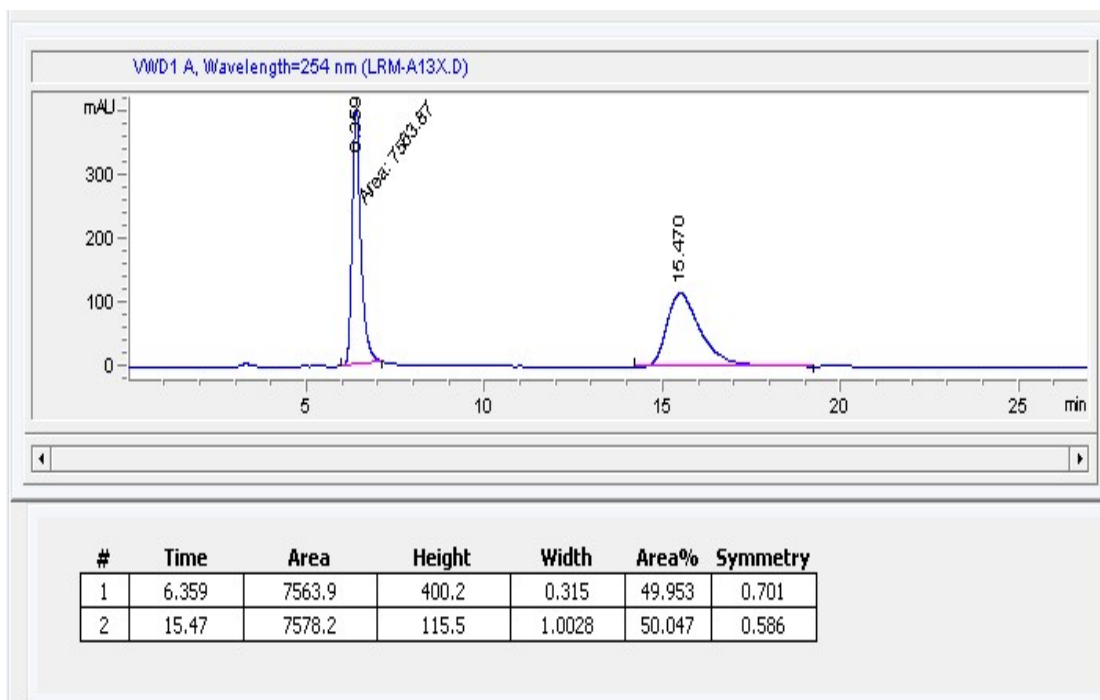
HPLC of 3p



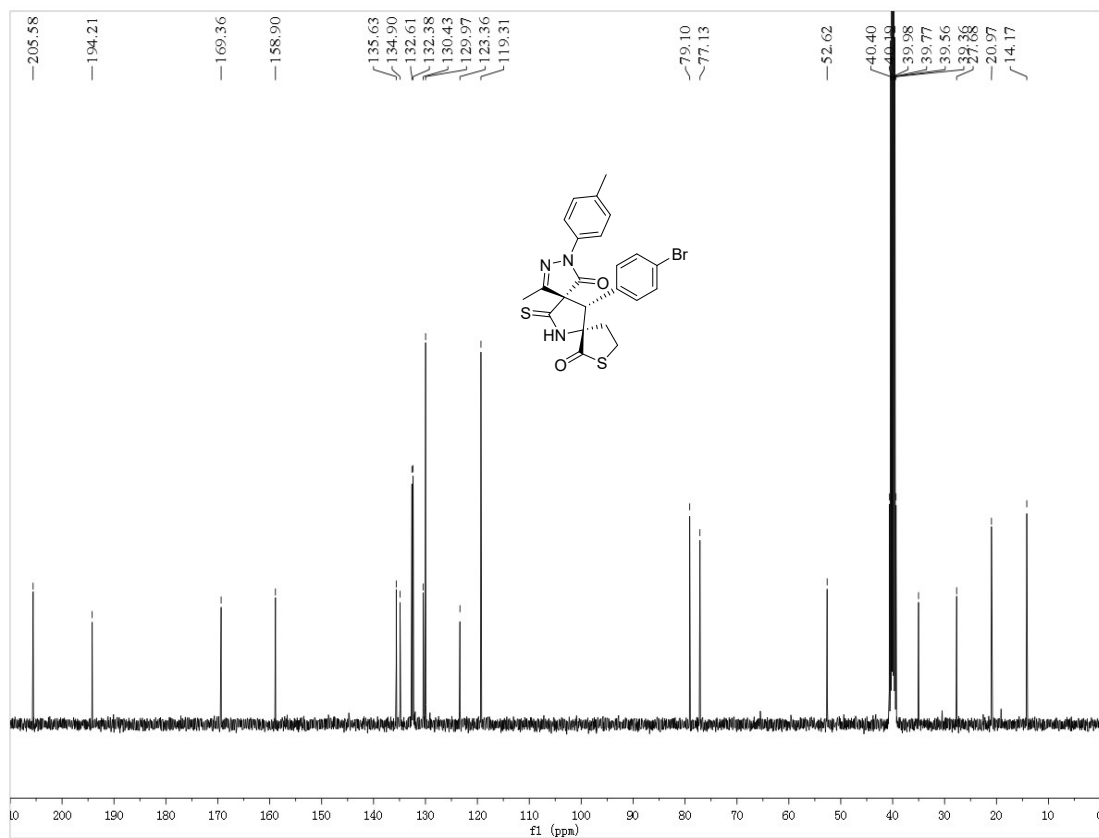
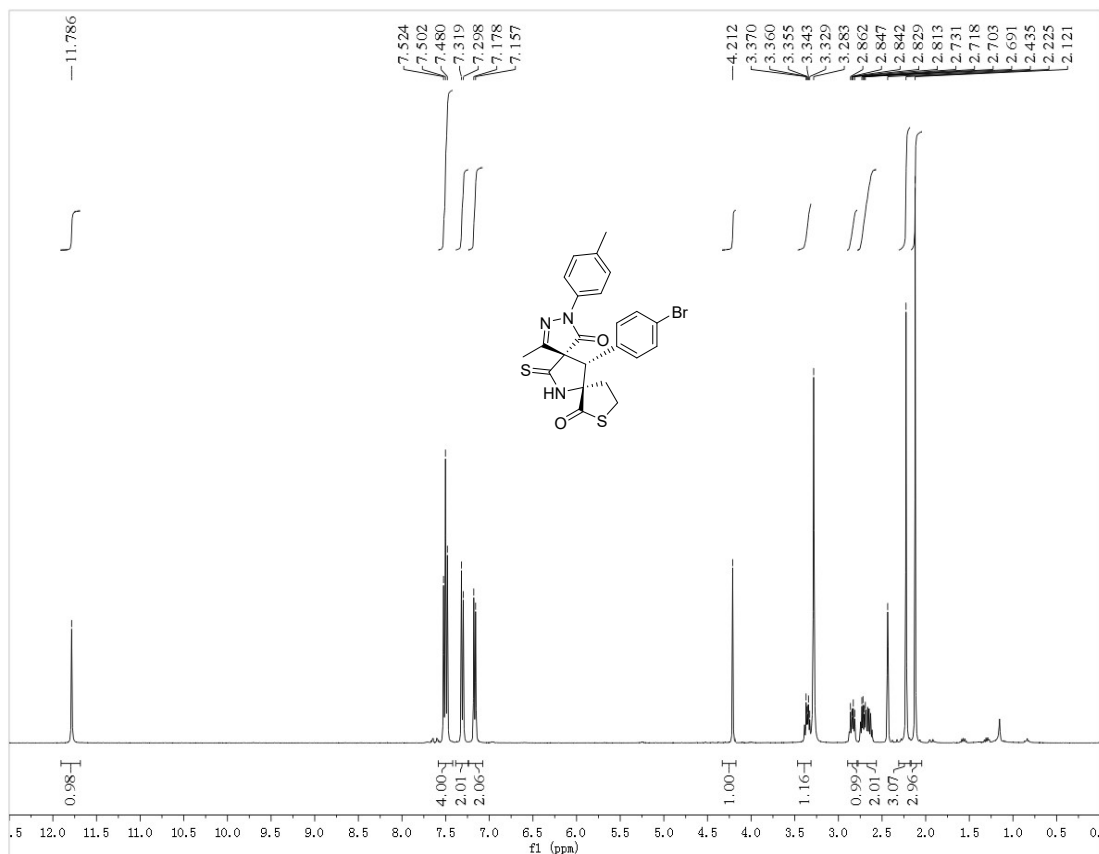
¹H and ¹³C NMR of 3q



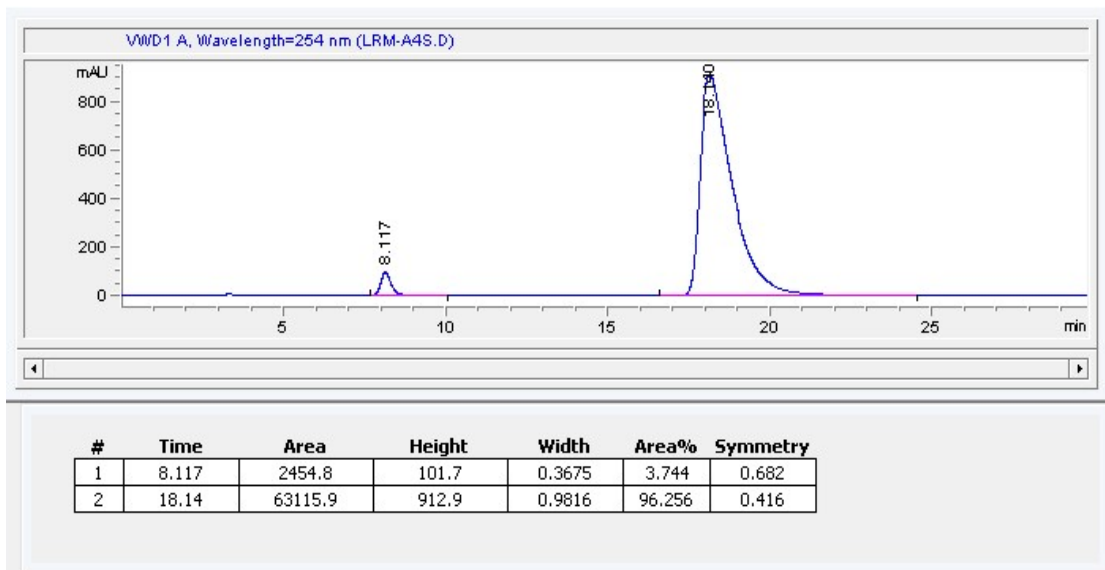
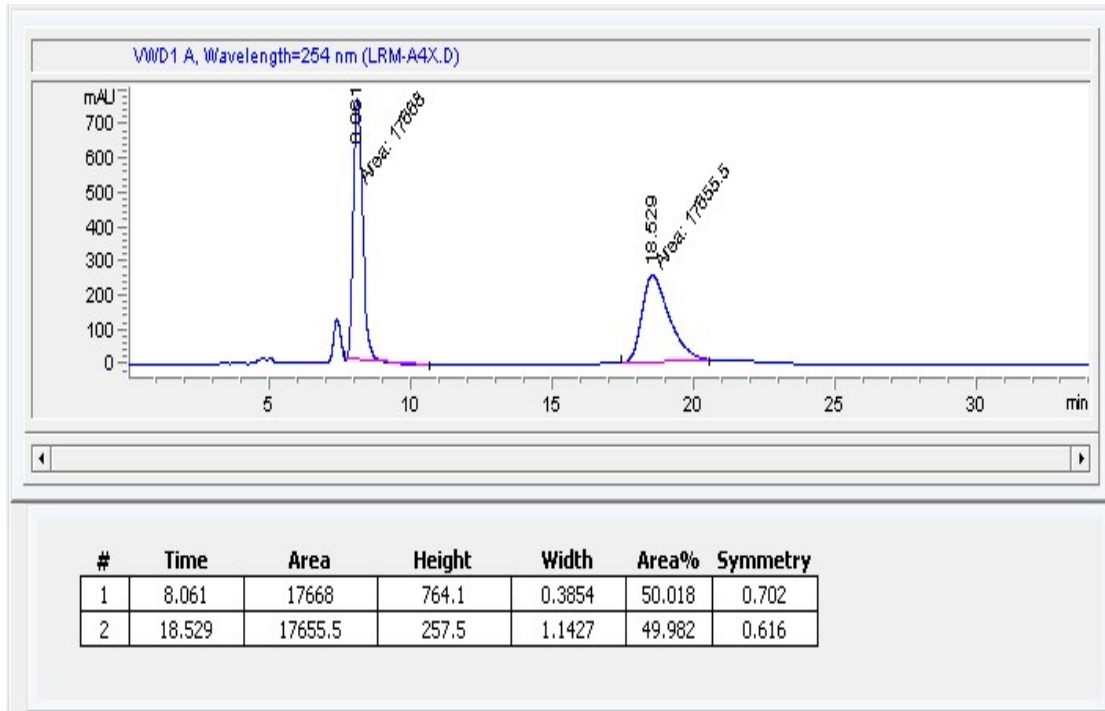
HPLC of 3q



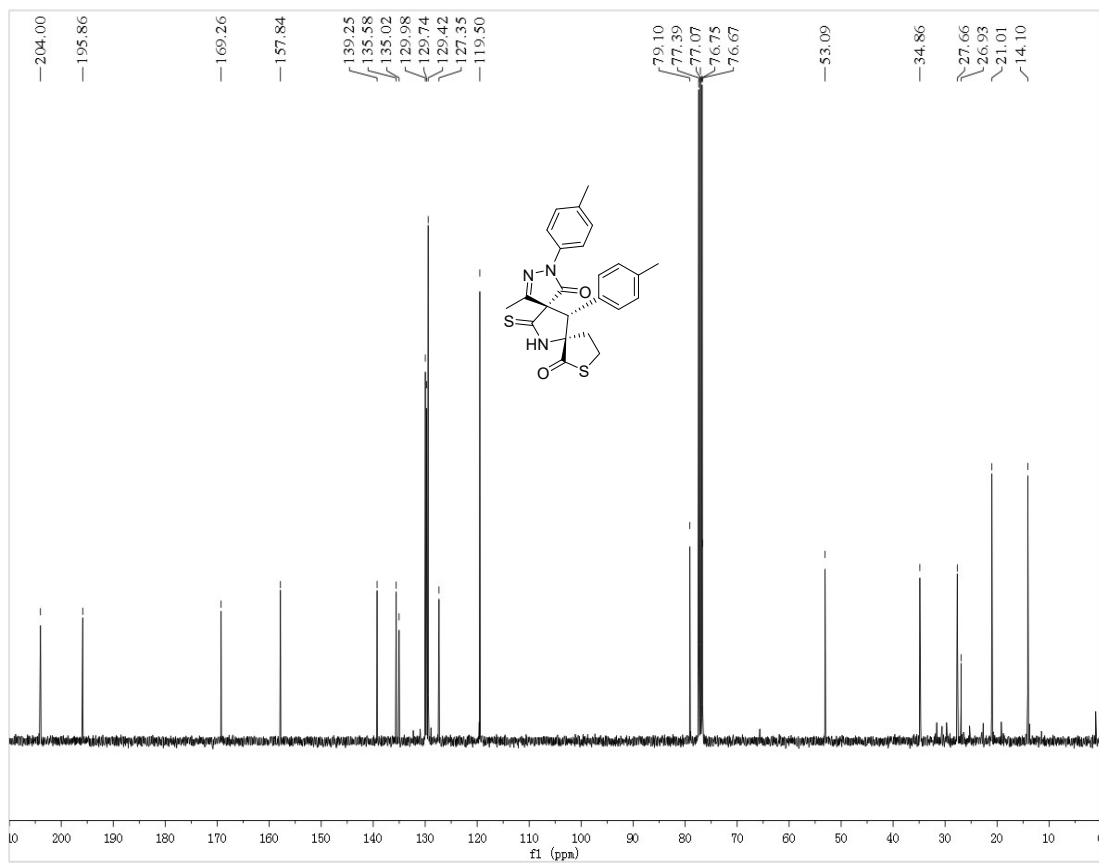
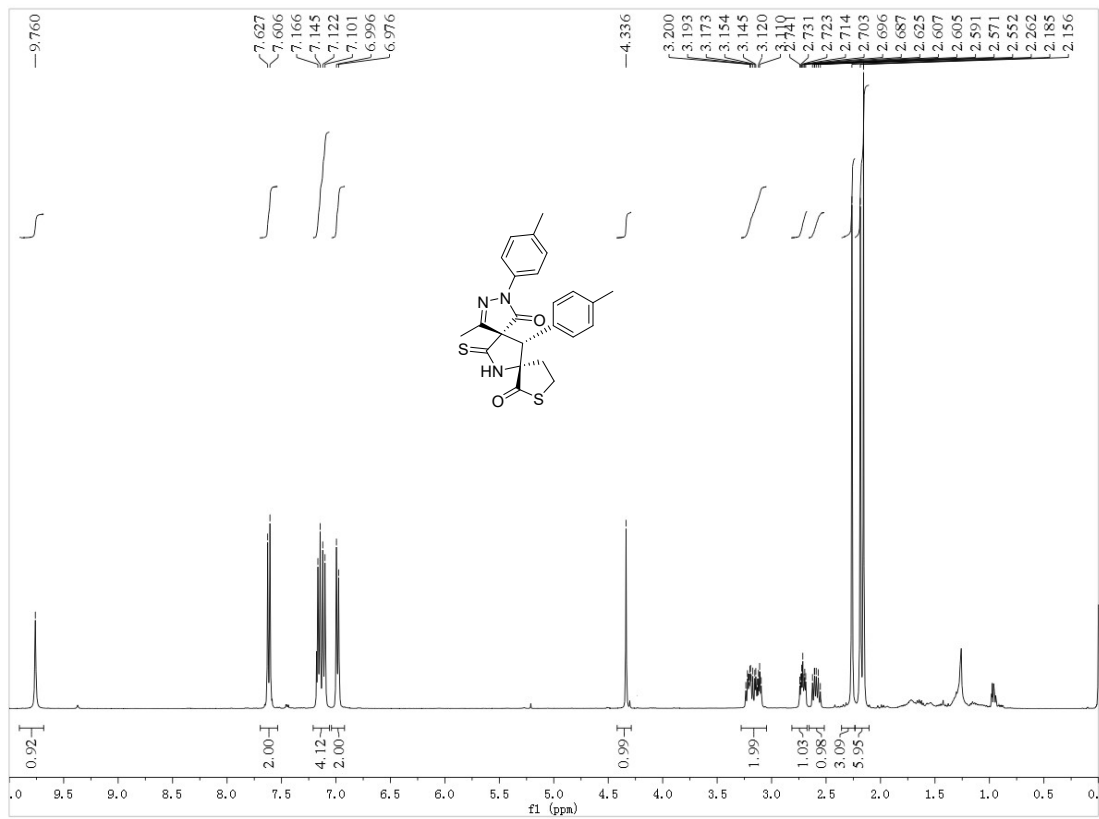
¹H and ¹³C NMR of 3r



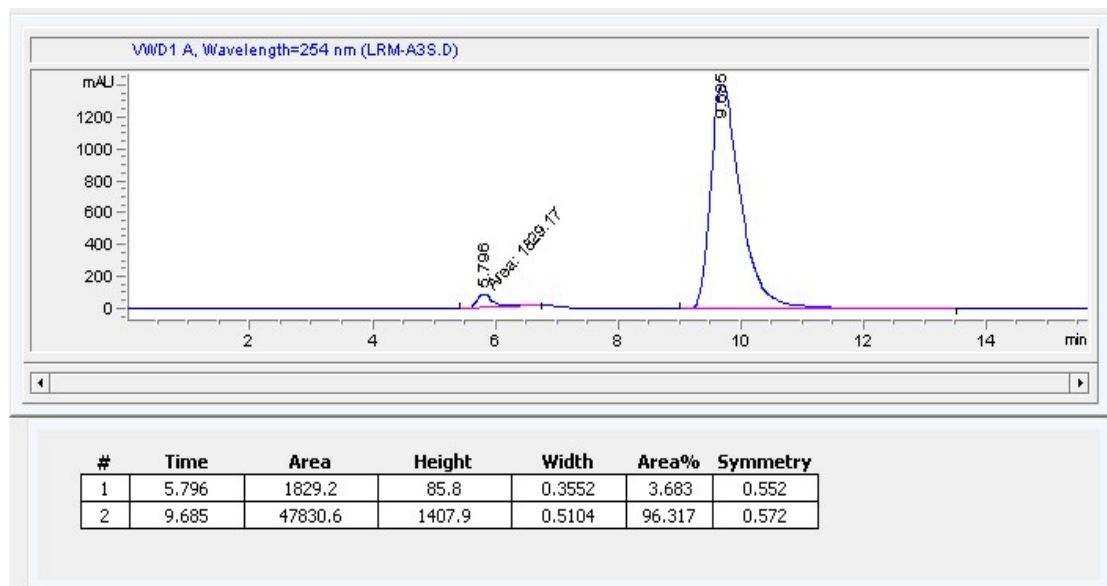
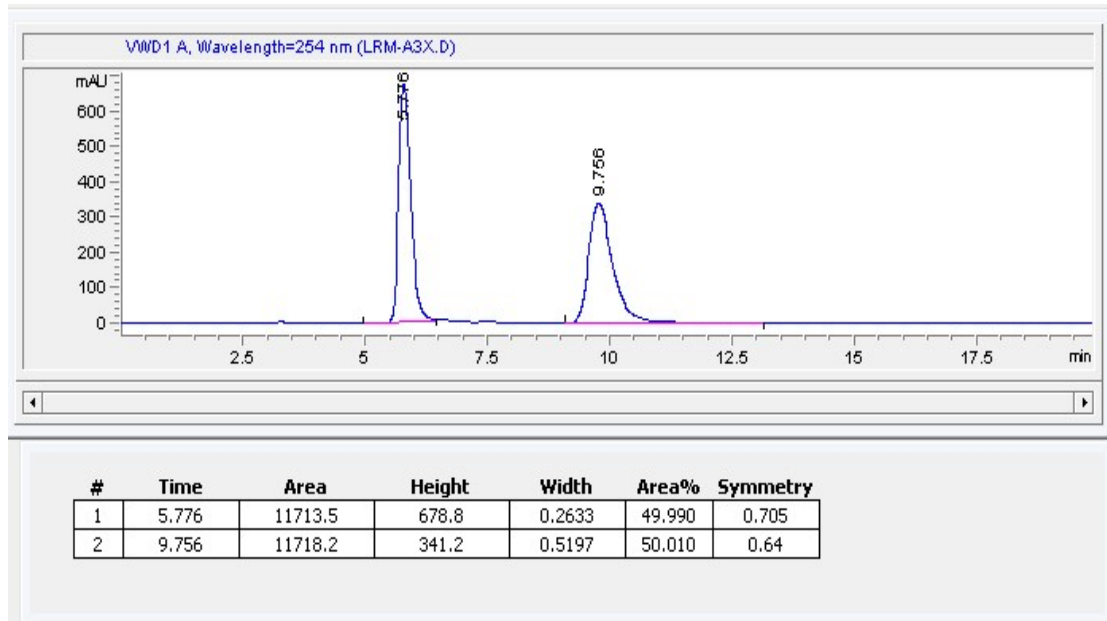
HPLC of 3r



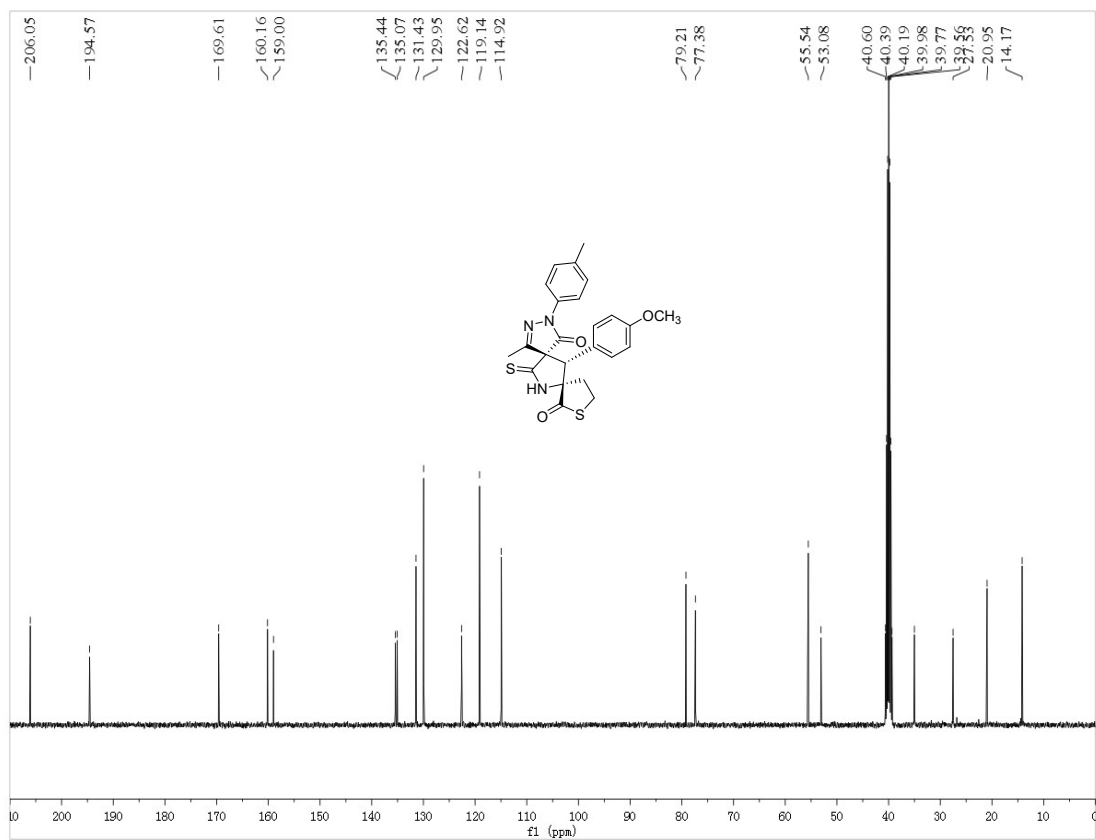
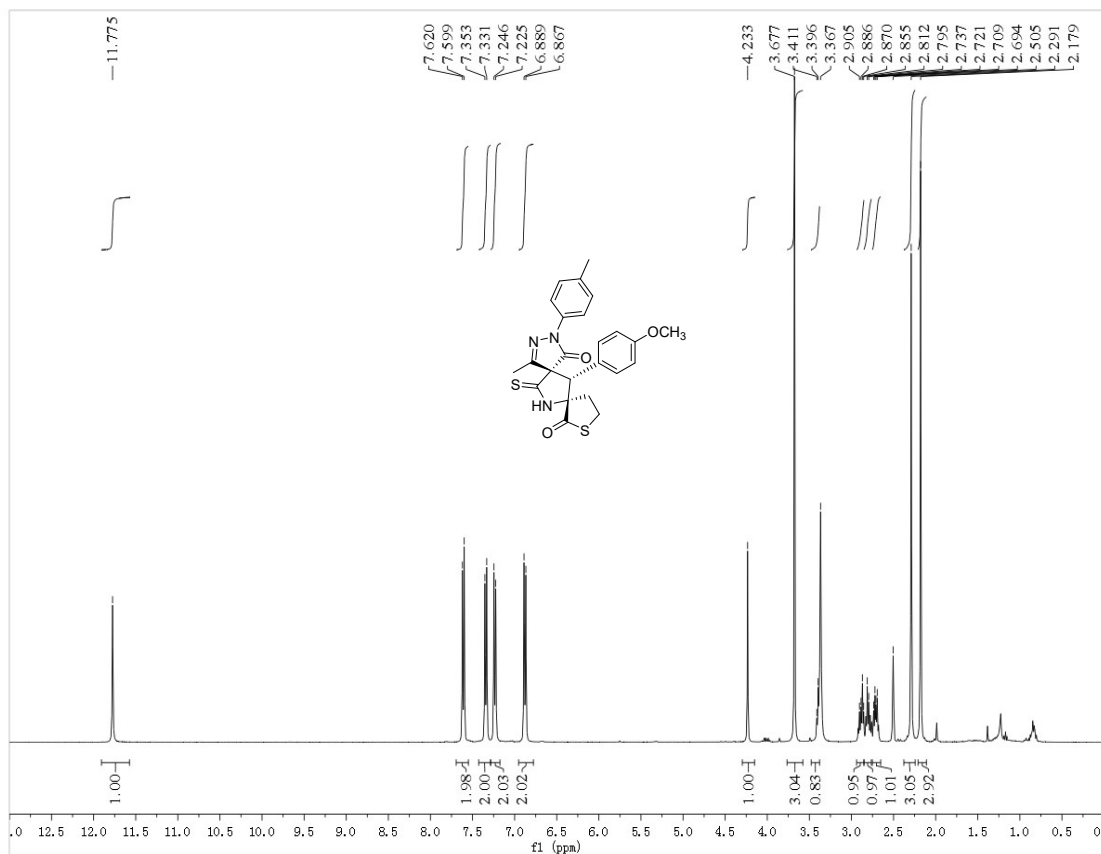
¹H and ¹³C NMR of 3s



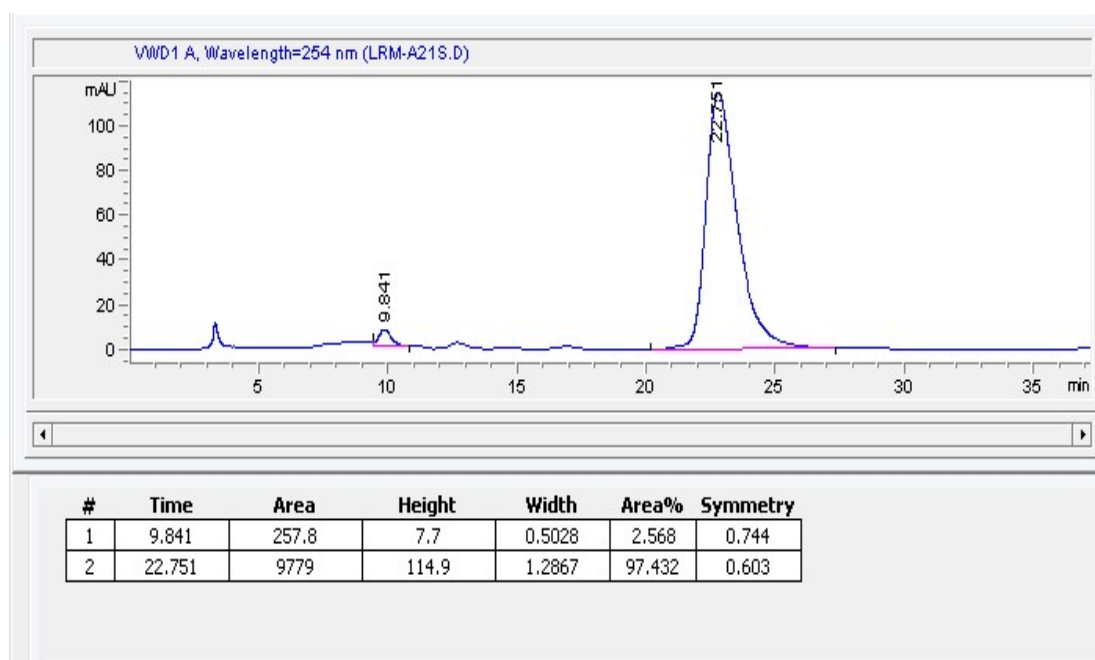
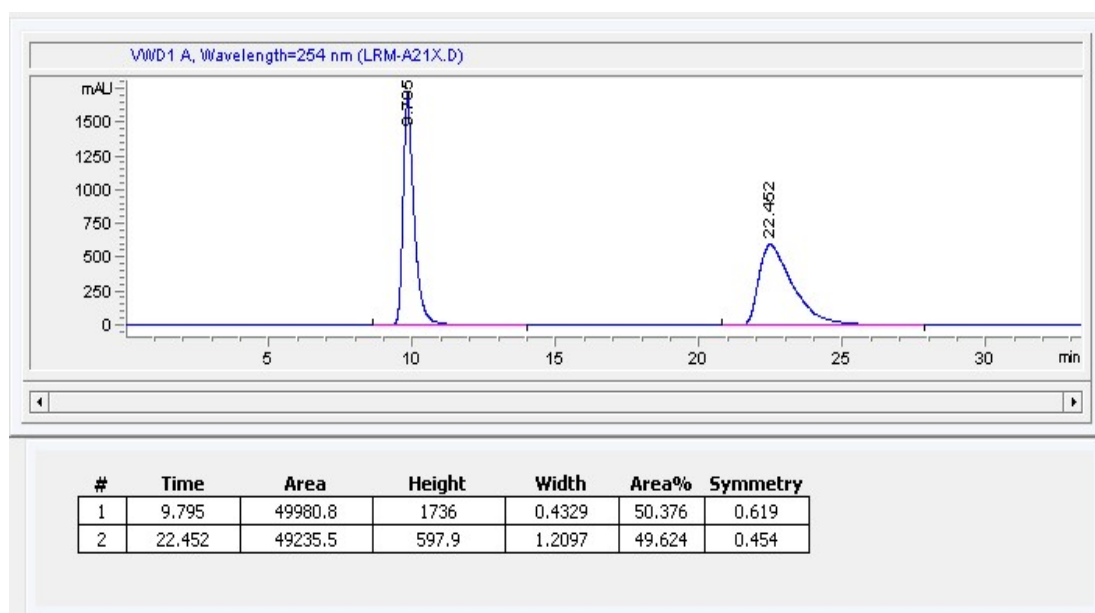
HPLC of 3s



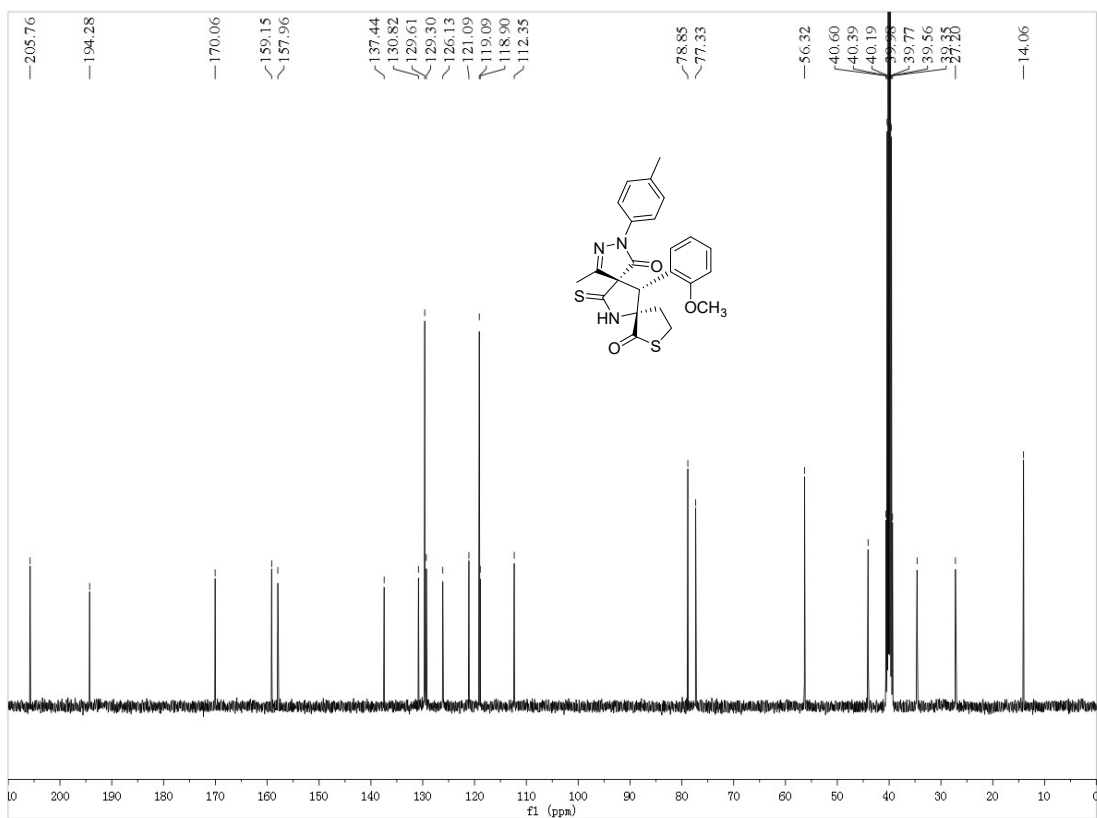
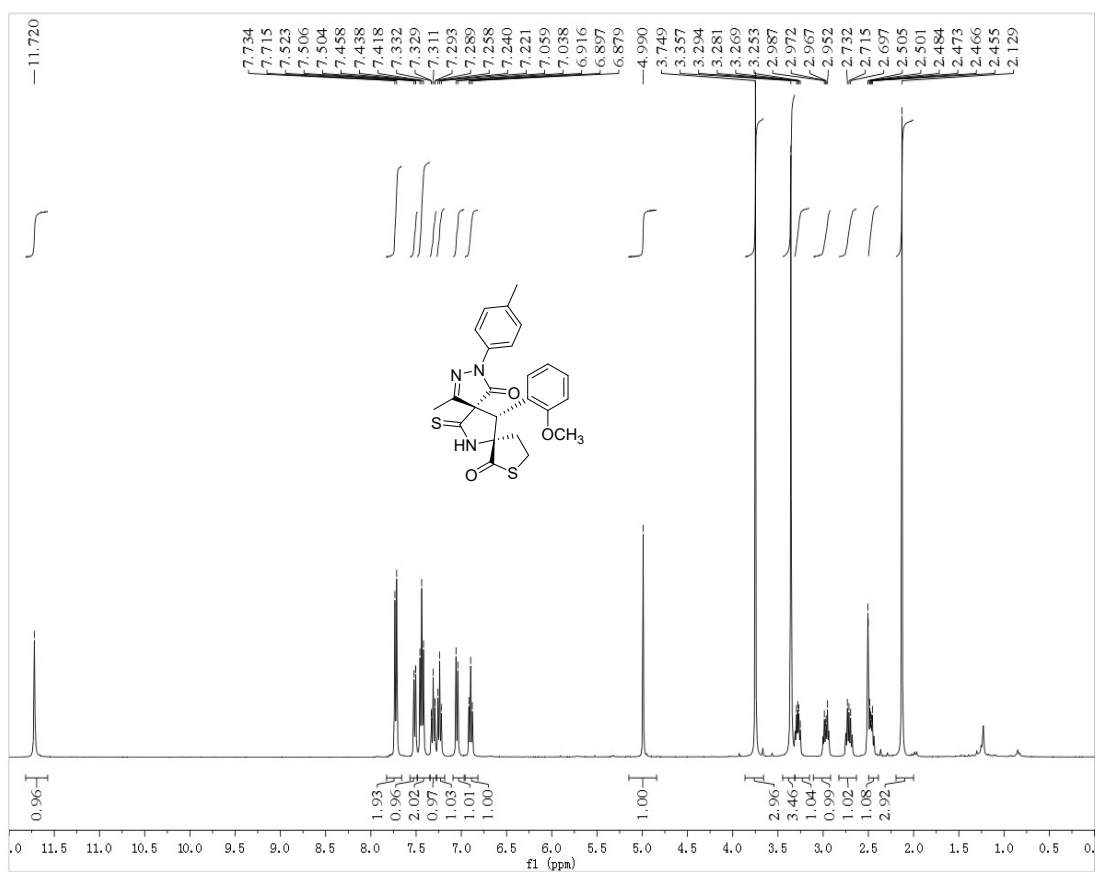
¹H and ¹³C NMR of 3t



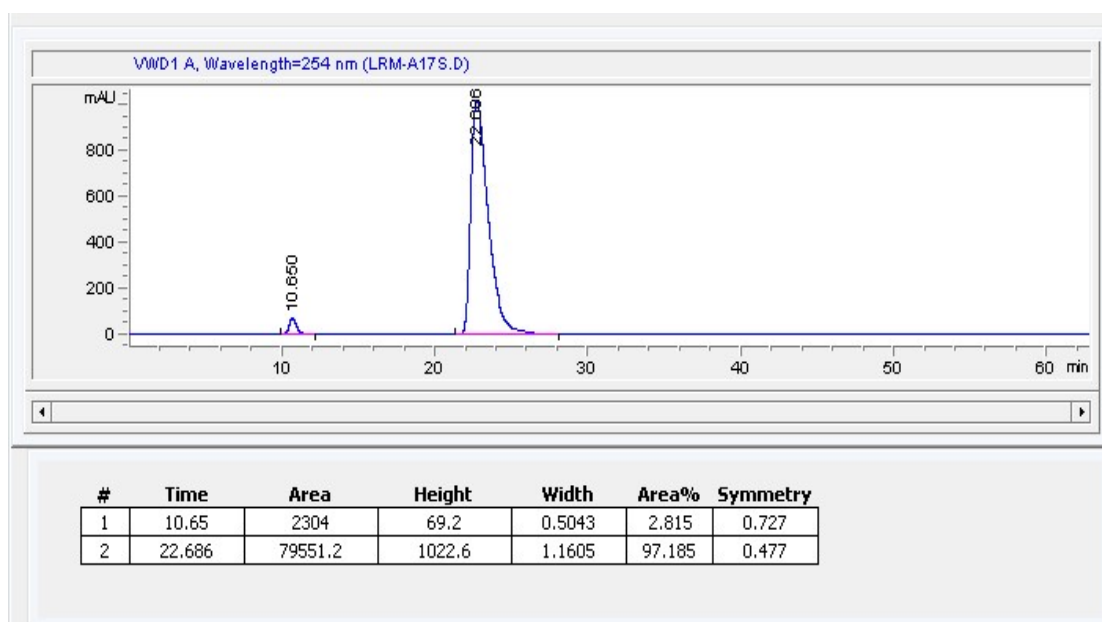
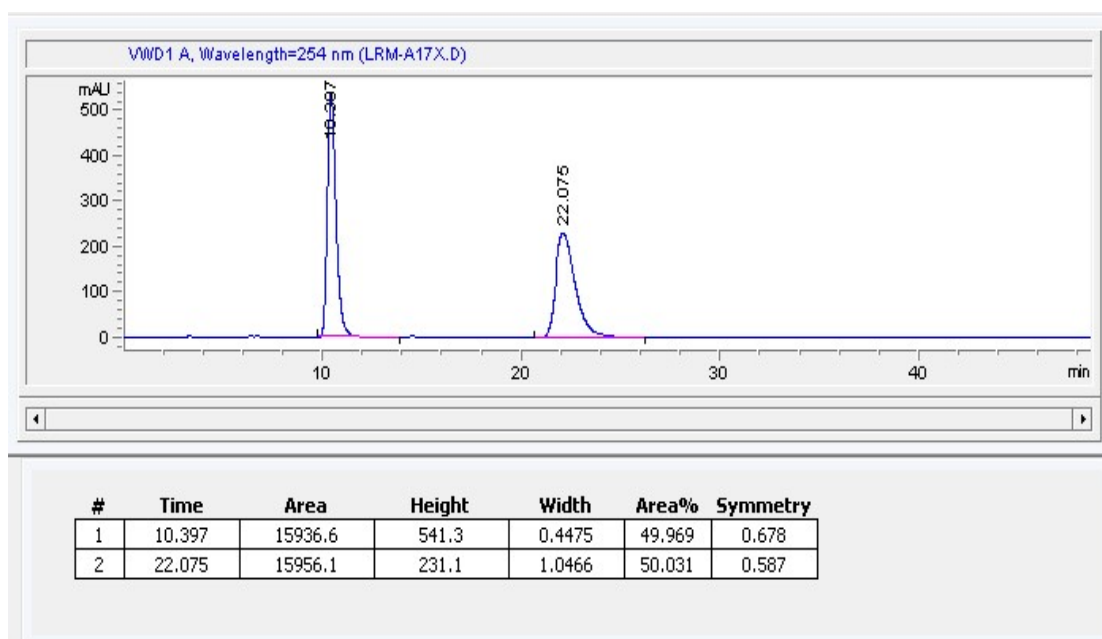
HPLC of 3t



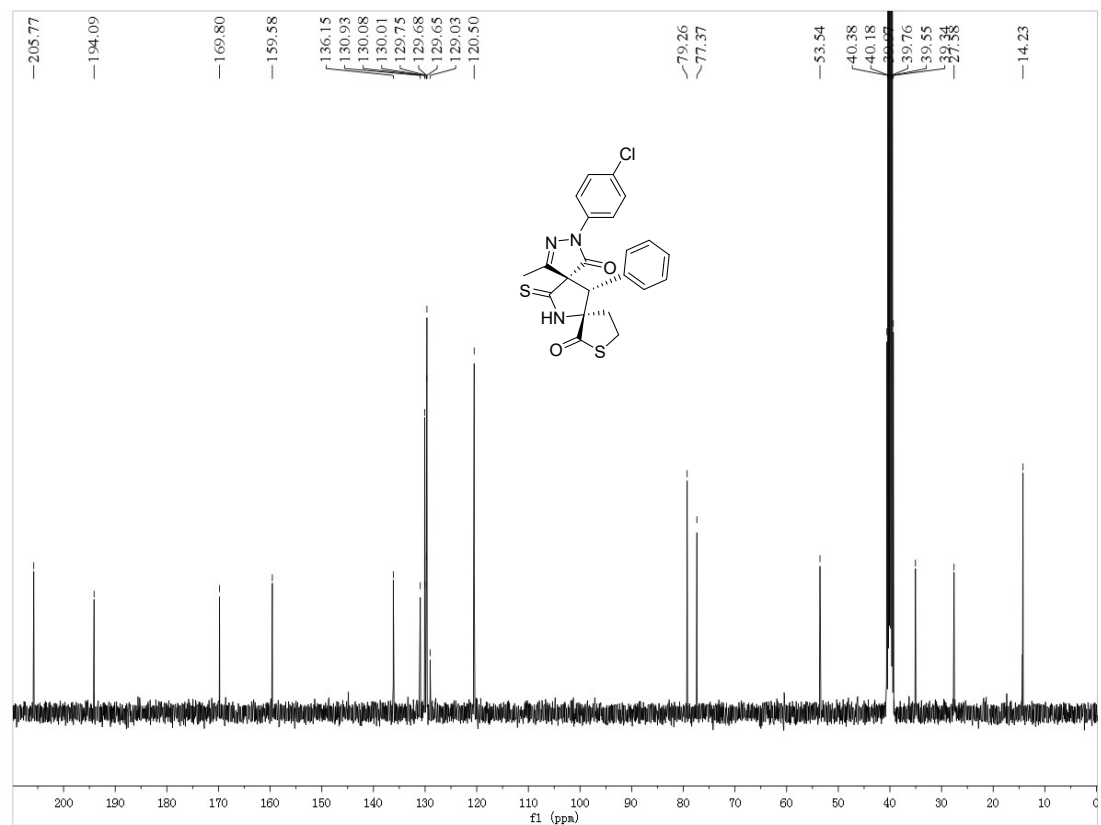
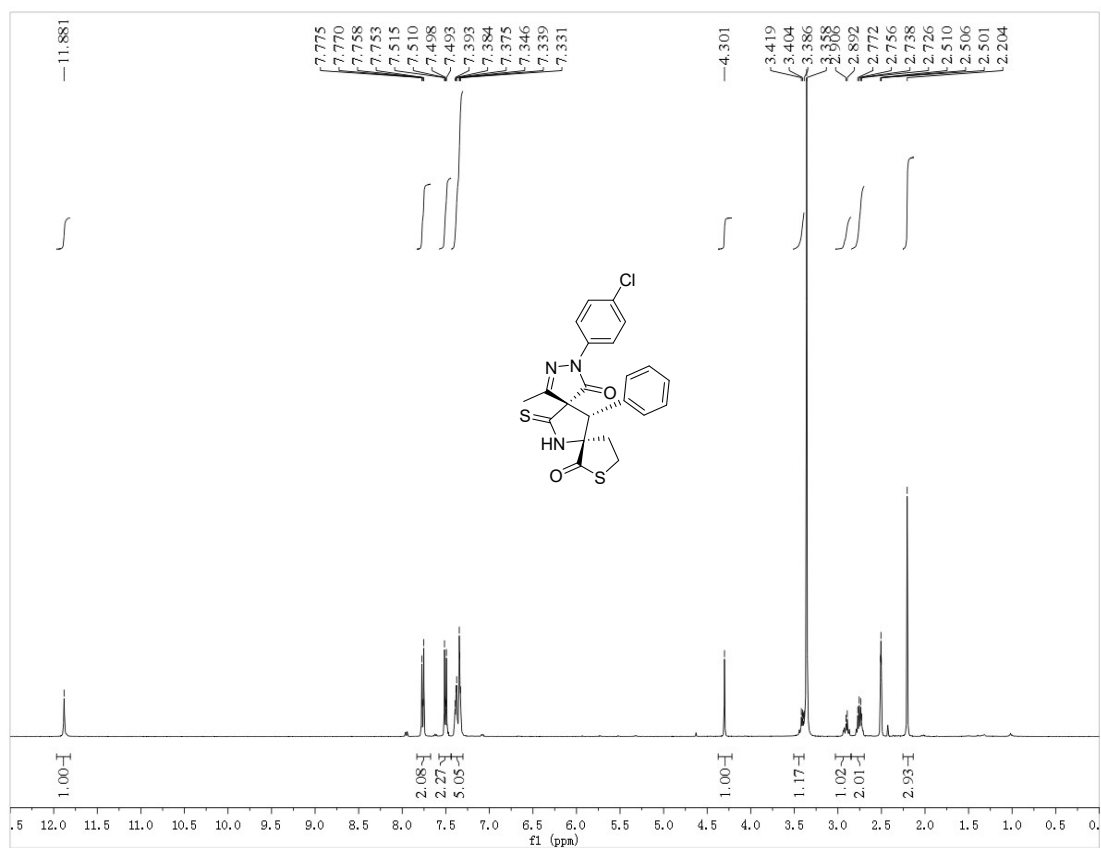
¹H and ¹³C NMR of 3u



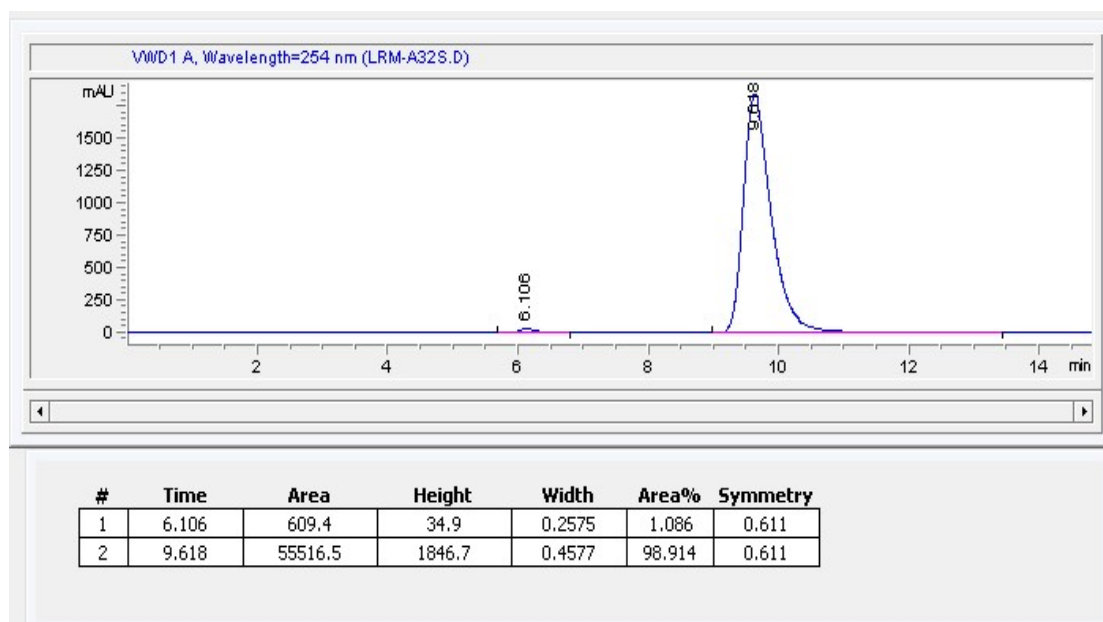
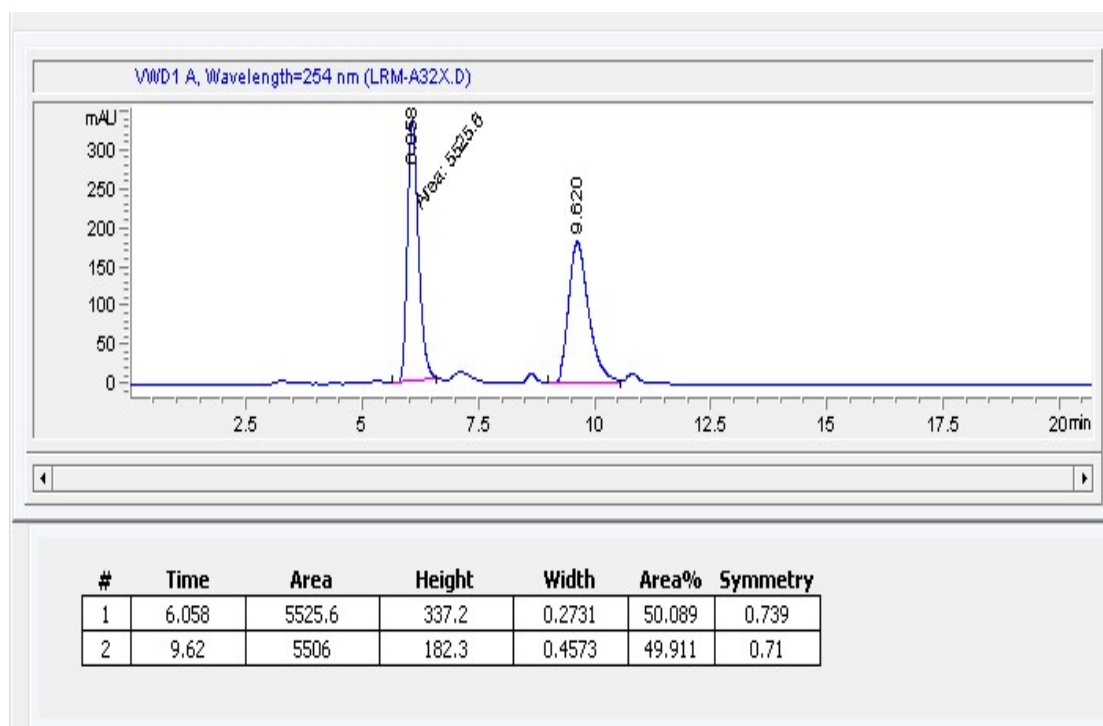
HPLC of 3u



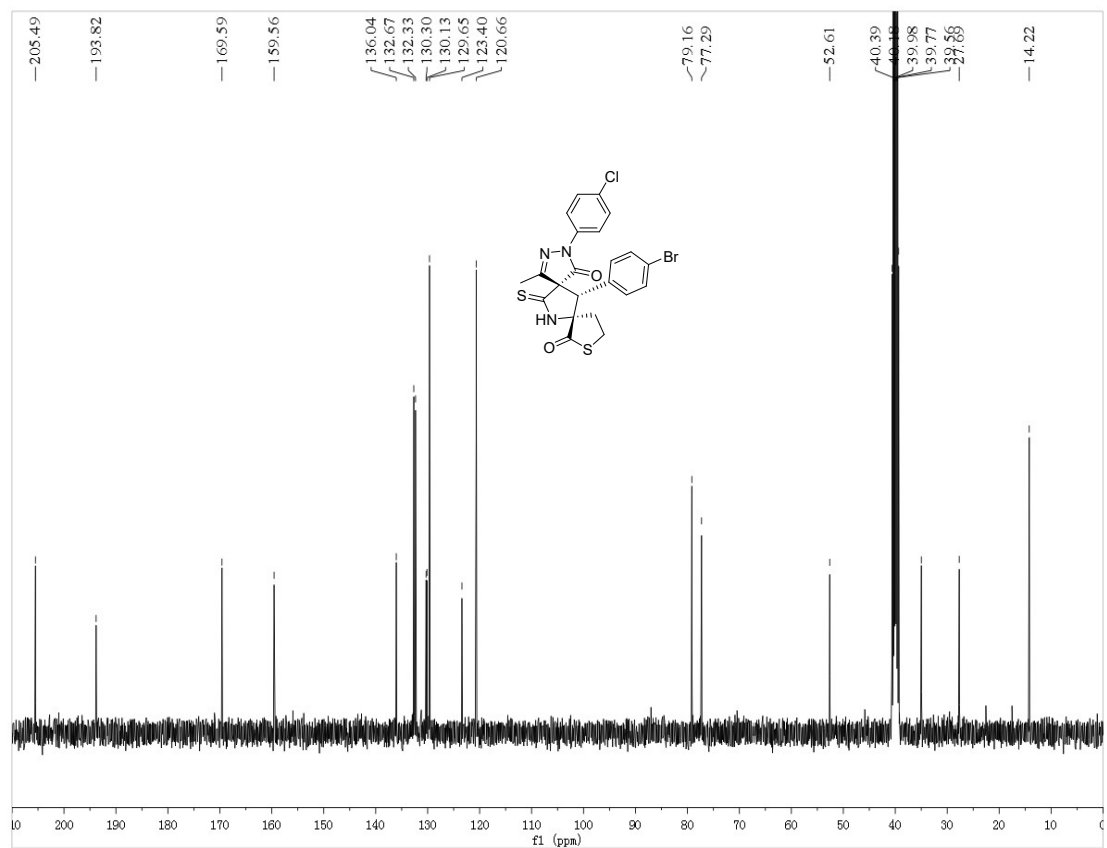
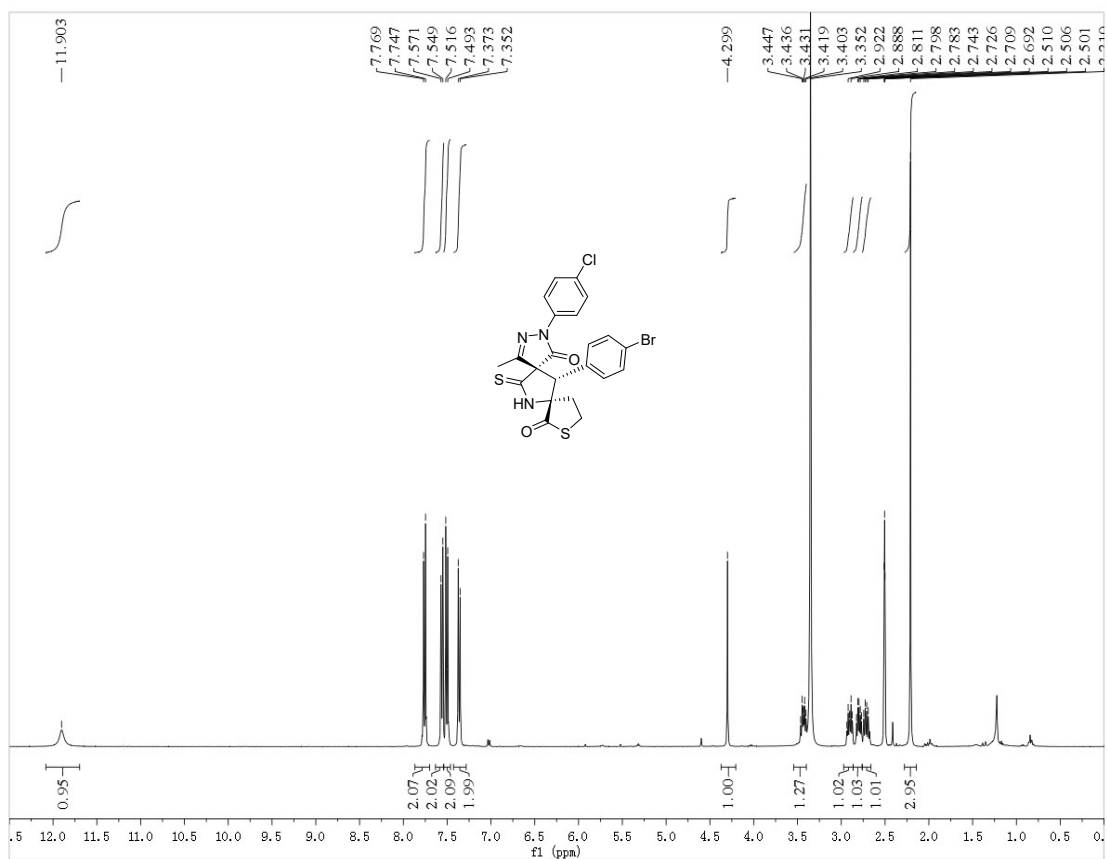
¹H and ¹³C NMR of 3v



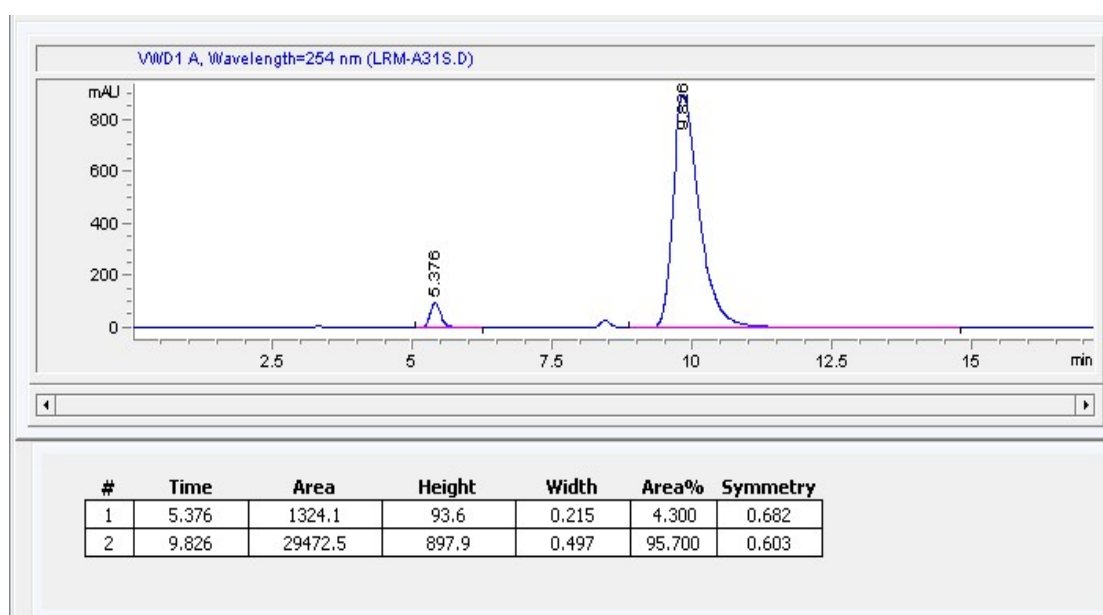
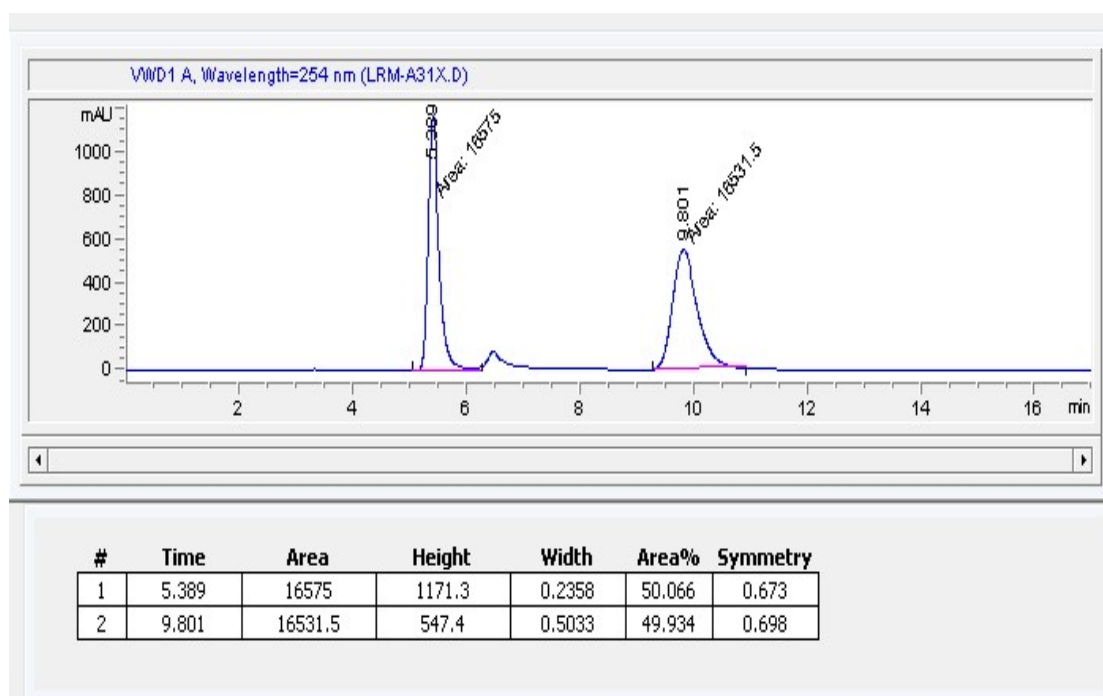
HPLC of 3v



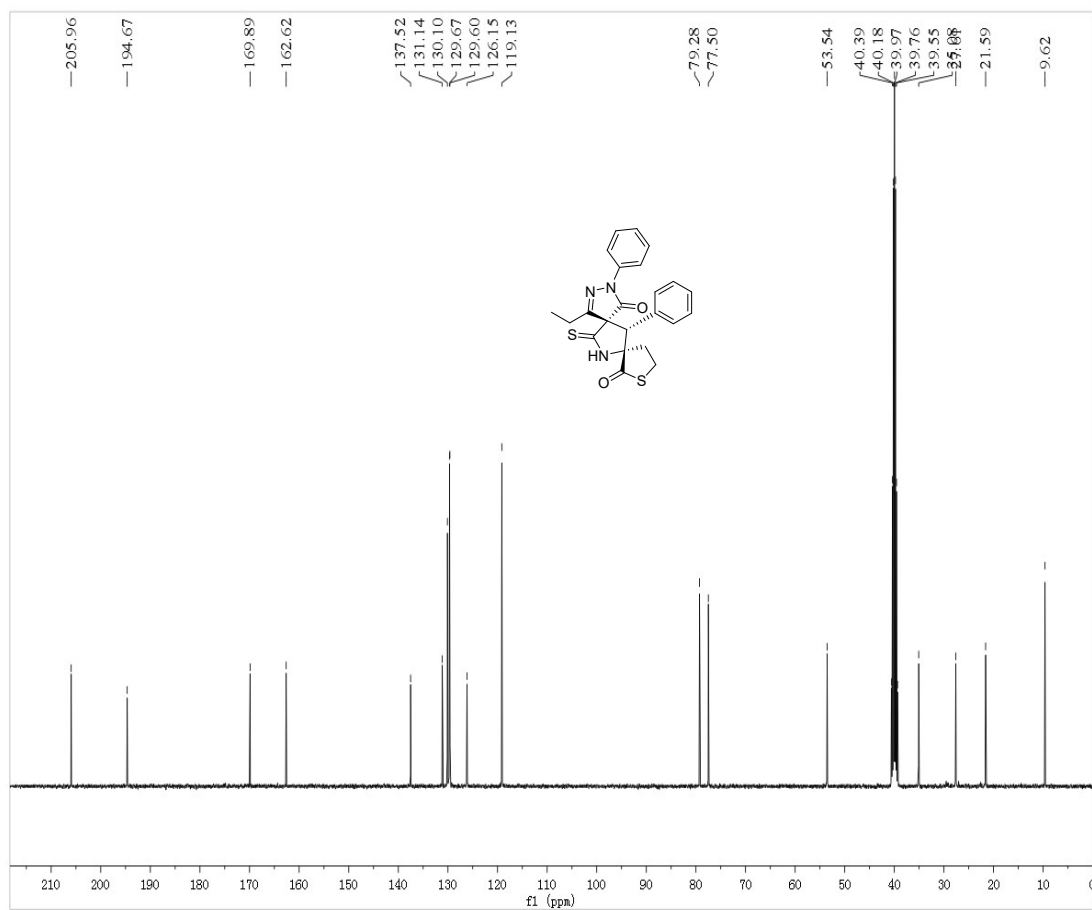
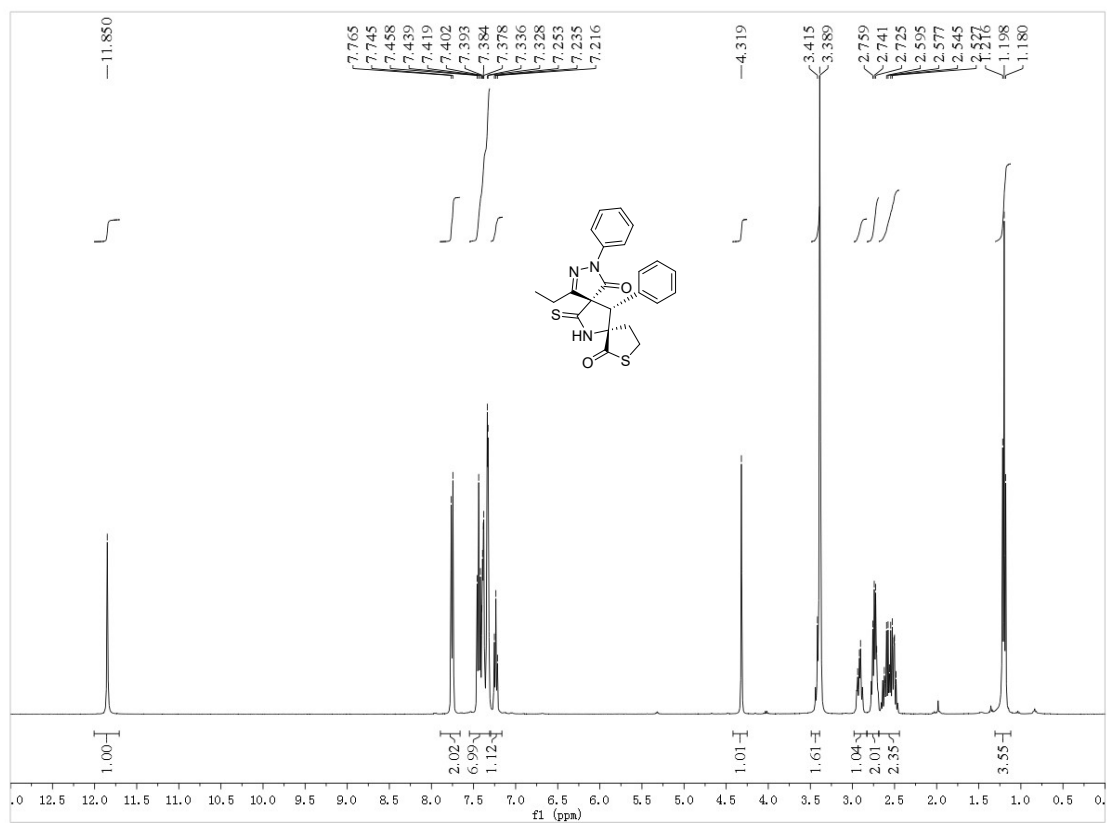
¹H and ¹³C NMR of 3w



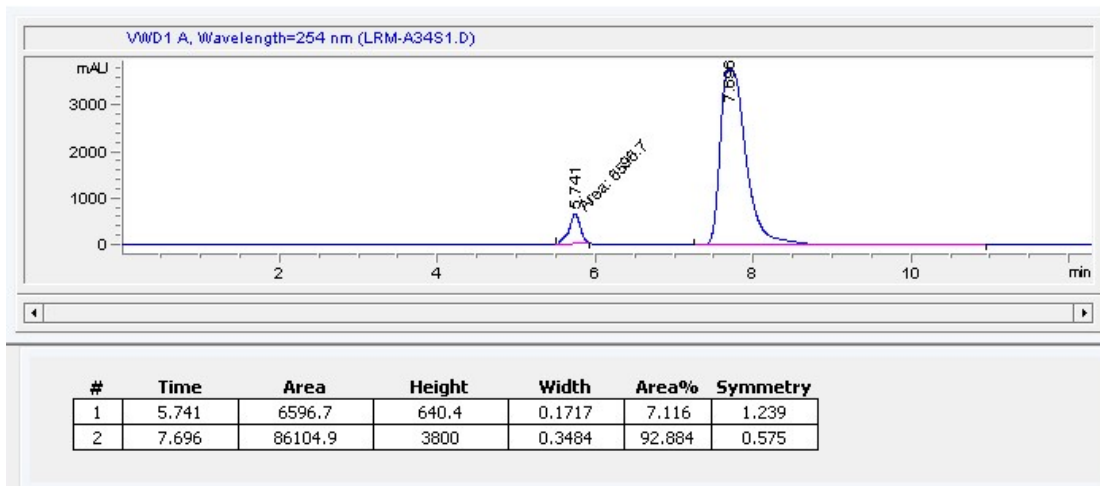
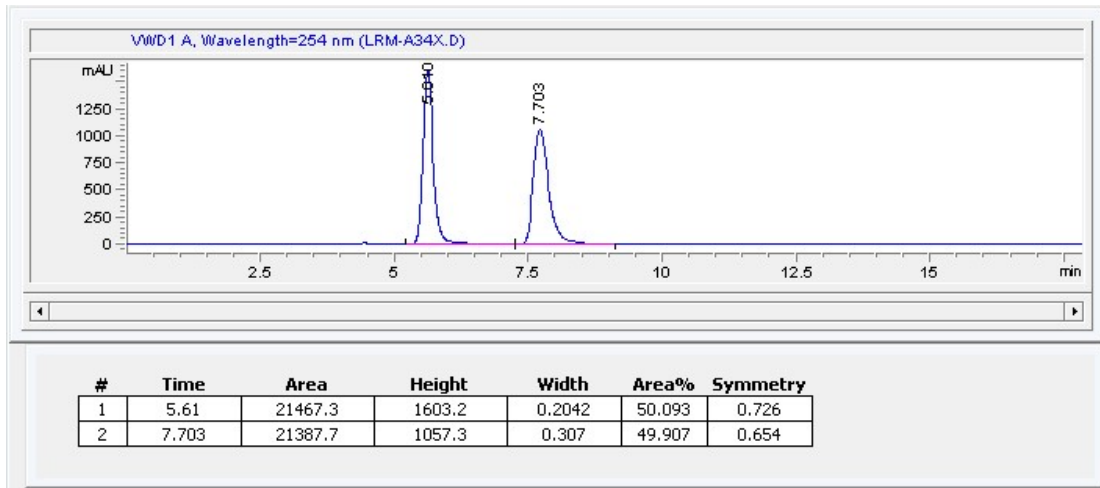
HPLC of 3w



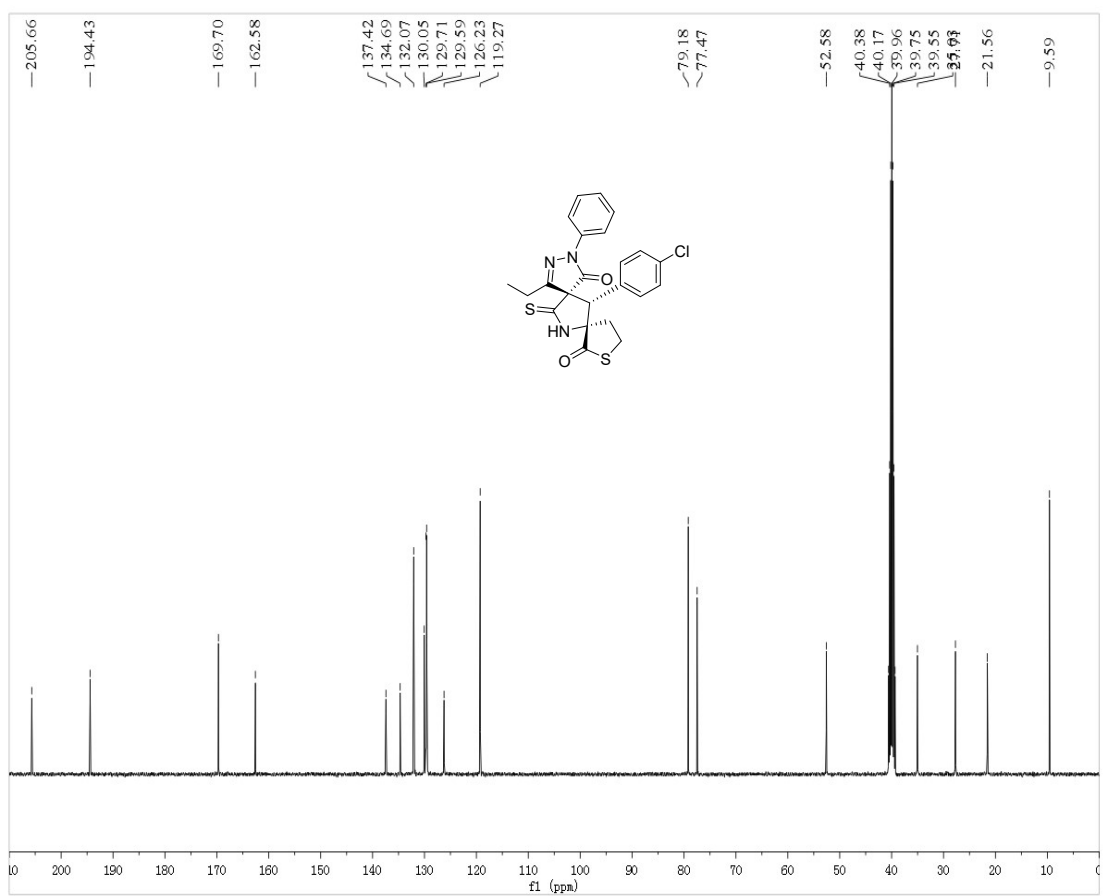
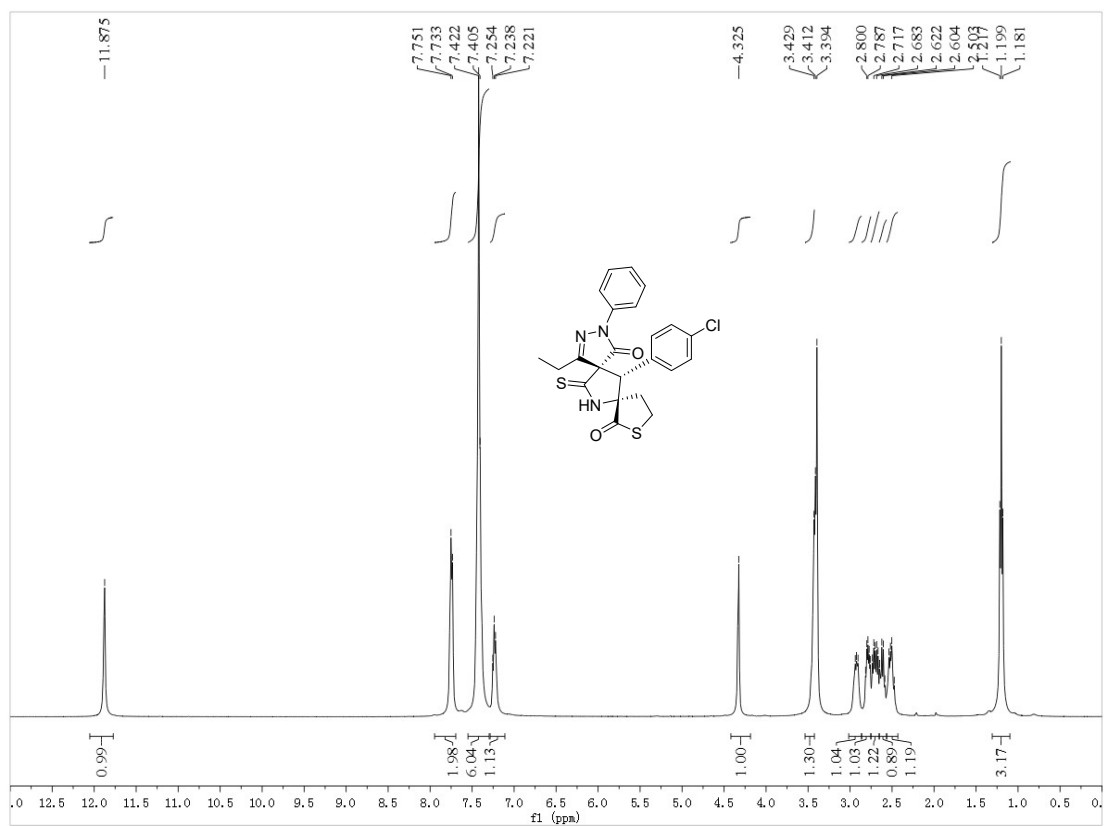
¹H and ¹³C NMR of 3x



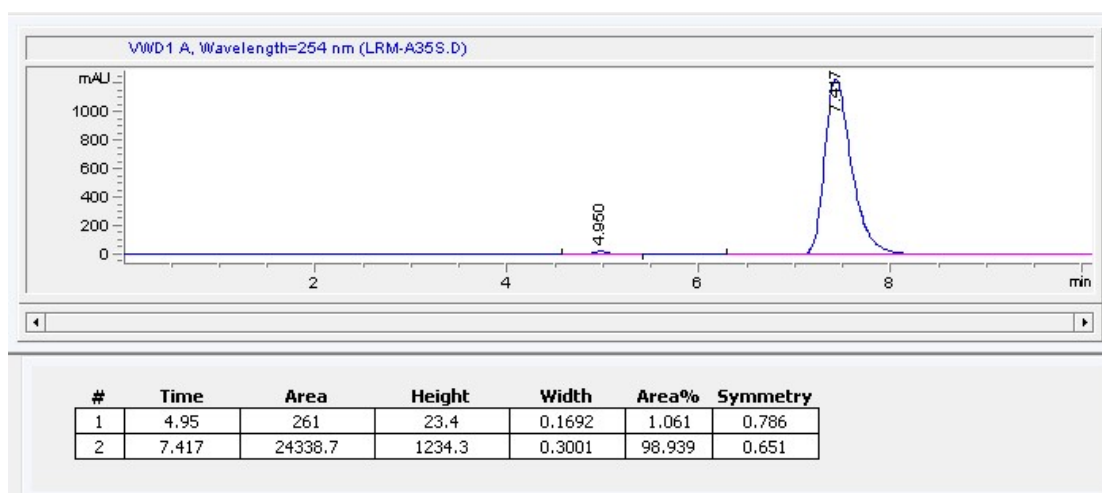
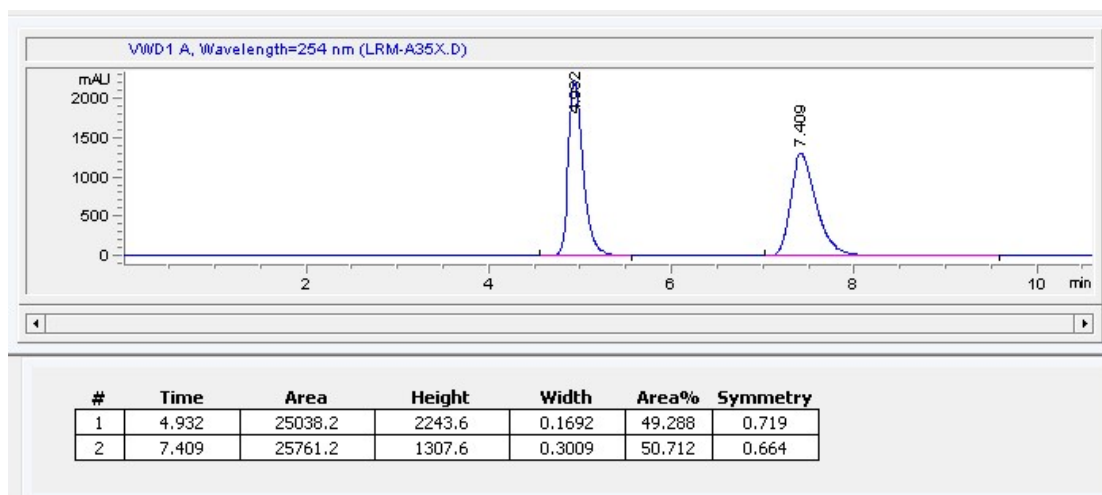
HPLC of 3x



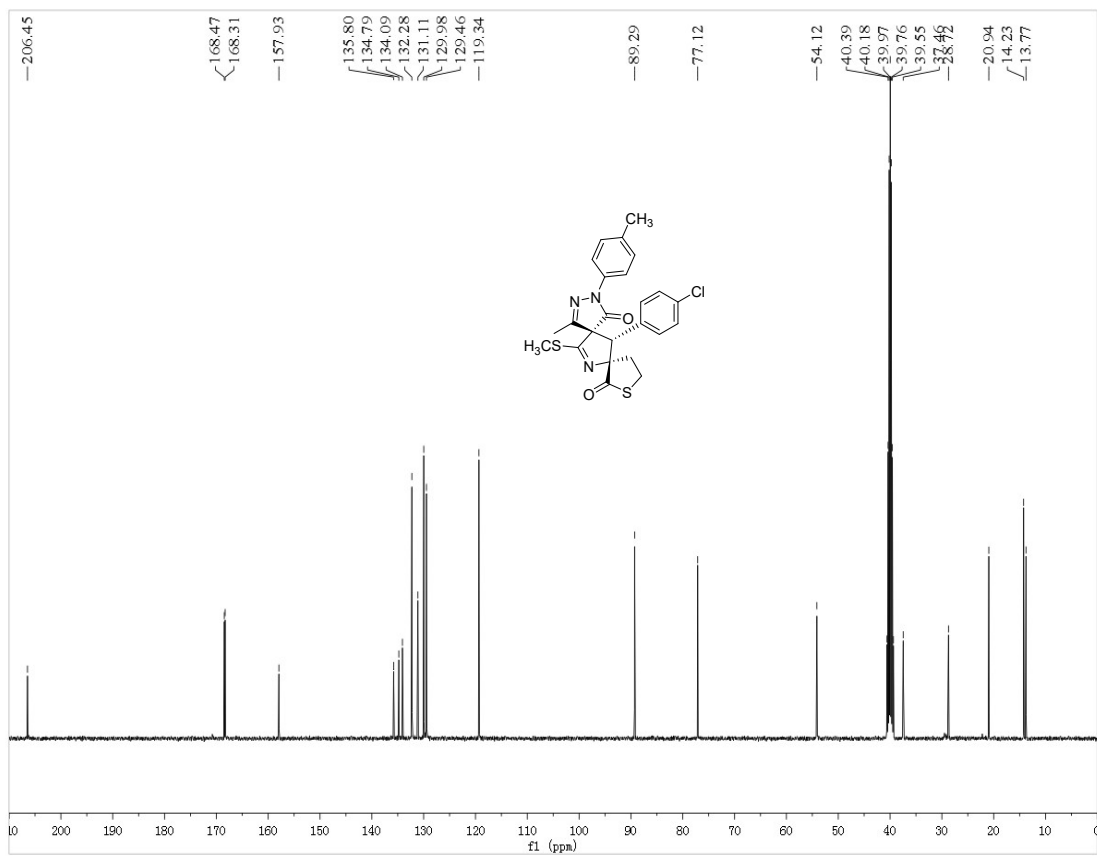
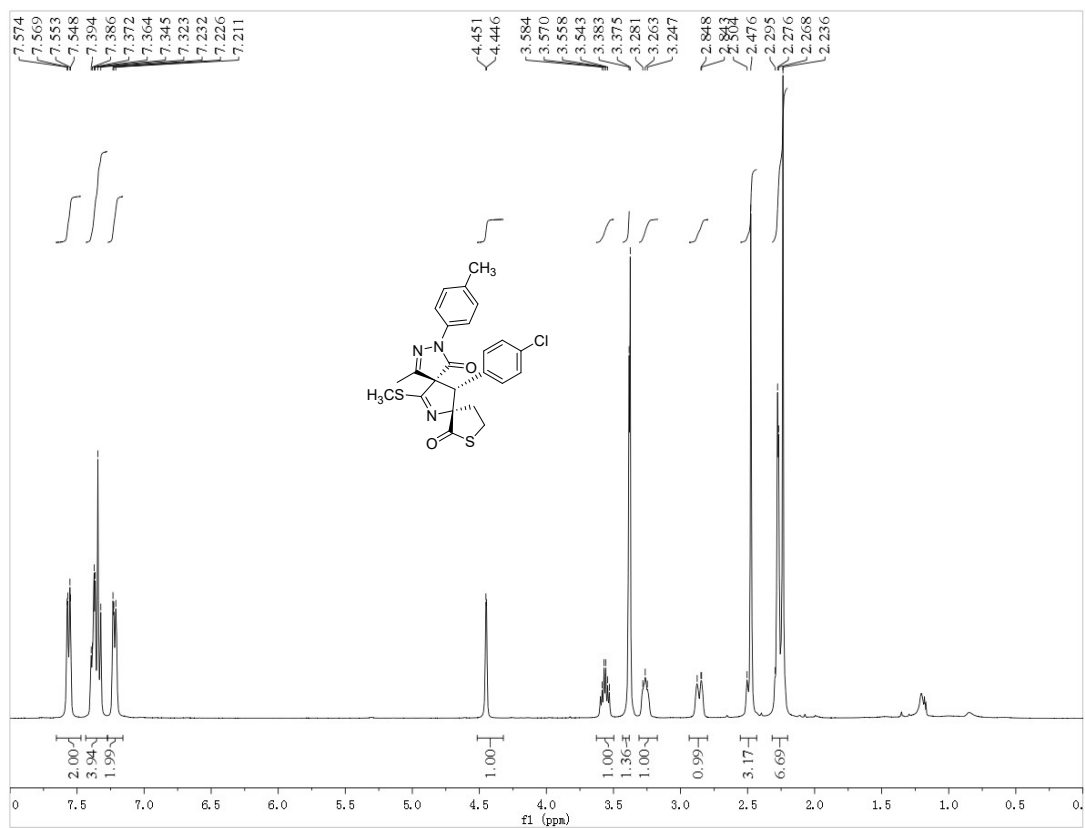
¹H and ¹³C NMR of 3y



HPLC of 3y



¹H and ¹³C NMR of 4q



HPLC of 4q

