

**Squaramide–Catalysed Asymmetric Michael Addition/Cyclization Cascade
Reaction of 4-Arylmethylidene-2,3-dioxopyrrolidines with 2-isothiocyanato-1-
indanones for Synthesis of Spiropyrolidinones**

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Supporting Information

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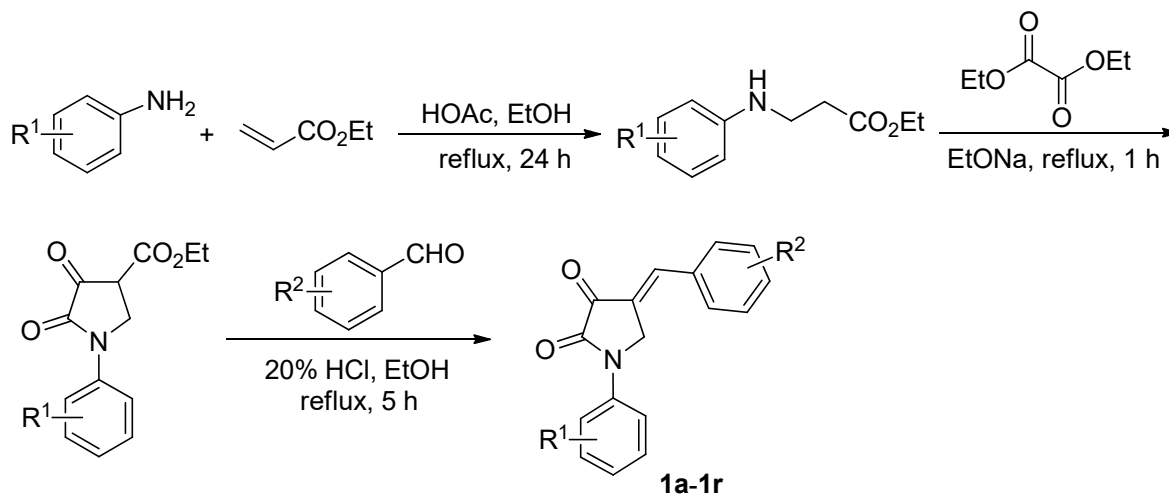
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1. General information and starting materials

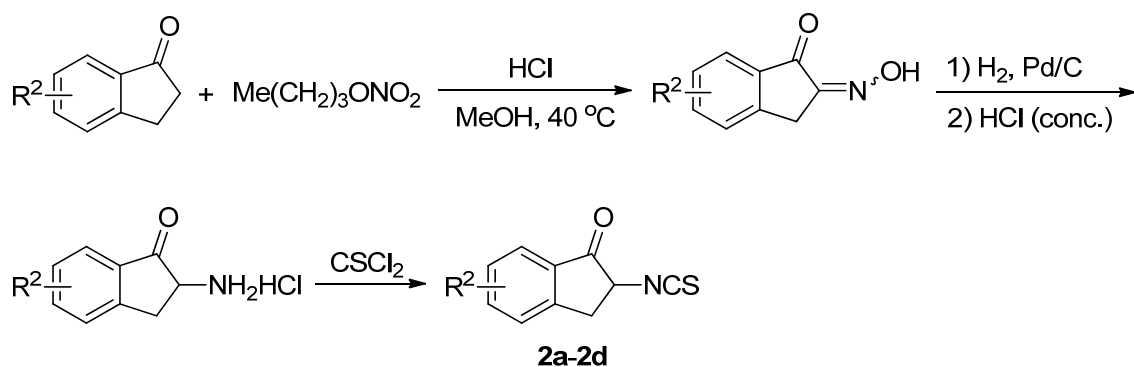
Commercially available compounds were used without further purification. Solvents were dried according to standard procedures. Column chromatography was performed with silica gel (200-300 mesh). Melting points were determined with an XT-4 melting-point apparatus and are uncorrected. ^1H NMR spectra were measured with Bruker Ascend 400 MHz spectrometer in CDCl_3 , chemical shifts were reported in δ (ppm) units relative to tetramethylsilane (TMS) as the internal standard. ^{13}C NMR spectra were measured at 100 MHz (Bruker Ascend 400 MHz spectrometer), chemical shifts were reported in ppm relative to TMS with the solvent resonance as internal standard (CDCl_3 , $\delta(\text{C}) = 77.00$ ppm; $\text{DMSO}-d_6$, $\delta(\text{C}) = 39.43$ ppm). Proton coupling patterns are described as broad (br) singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). High resolution mass spectra were measured with an Agilent 6520 Accurate-Mass-Q-TOF MS system equipped with an electrospray ionization (ESI) source. Enantiomeric excesses were determined by chiral HPLC analysis using an Agilent 1200 LC instrument with a Daicel Chiralpak IA, IC or AD-H column.

2. General procedures for the preparation of substrates.

The 4-arylmethylidene-2,3-dioxopyrrolidines **1a-1r** were prepared according to the reported literature procedures.¹

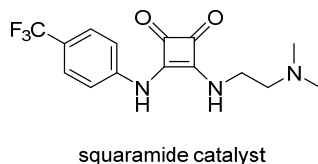


The 2-isothiocyanato-1-indanones **2a-2d** were prepared according to the reported literature procedures.²



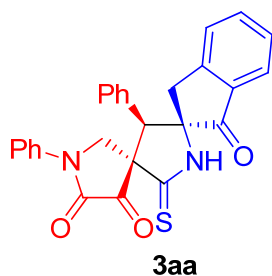
3. Procedure for the synthesis of racemates of **3**

To a dried small bottle were added **2** (0.12 mmol, 1.2 equiv.), **1** (0.1 mmol, 1.0 equiv.) and squaramide catalyst (10 mol%) in 1.0 ml of DCM, the mixture was stirred at room temperature overnight. When the reaction completed detected by TLC, the reaction mixture was concentrated and directly purified by silica gel column chromatography to afford the racemates of **3**.



4. Procedure for the synthesis of chiral compound **3**

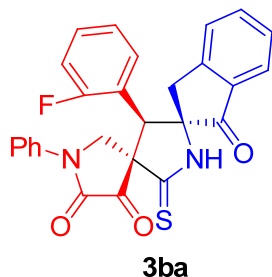
To a dried small bottle were added 2,3-dioxopyrrolidines **1** (0.1mmol), 2-isothiocyanato-1-indanone **2** (0.12 mmol), squaramide catalyst **C8** (5 mol%) in 2.0 mL of AcOEt at room temperature. The reaction mixture was stirred for 15 h and the progress of the reaction was monitored by TLC analysis (Petroleum ether/ ethyl acetate = 1:1). After the completion of the reaction, the crude product mixture was purified by flash column chromatography on silica (petroleum ether/ethyl acetate = 5:1–3:1) to afford the pure product **3**.



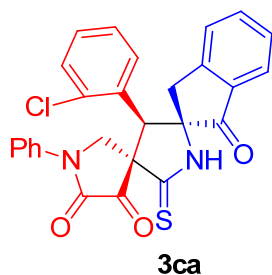
(2*R*,3'*R*,4'*S*)-1'',3'-Diphenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-

1,4'',5'''(3*H*)-trione (3aa**). **3aa** was obtained as a light yellow solid (42.5 mg, 94% yield), m.p. 230–232 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 75:25, flow rate 1.0 mL/min, detection at 254 nm): t_R = 12.0 min (minor), t_R = 24.0 min (major), 93% ee. $[\alpha]_D^{20}$ = -80.7 (c 0.62, CH_2Cl_2). $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 8.90 (s, 1H, NH), 7.78 (d, J = 7.6 Hz, 2H, ArH), 7.71 (d, J = 7.6 Hz, 1H, ArH), 7.58 (t, J = 7.2 Hz, 1H, ArH), 7.43 (t, J = 7.6 Hz, 2H, ArH), 7.36–7.28 (m, 3H, ArH), 7.19–7.12 (m, 3H, ArH), 6.95–6.93 (m, 2H, ArH), 4.92 (d, J = 10.8 Hz, NCH_2), 4.42 (s,**

1H, CH), 4.00 (d, $J = 10.8$ Hz, 1H, NCH₂), 3.86 (d, $J = 18.4$ Hz, CH₂), 3.66 (d, $J = 18.8$ Hz, CH₂) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 202.1, 199.2, 195.7, 155.9, 152.2, 138.1, 137.0, 133.9, 130.9, 129.31, 129.28, 129.1, 128.9, 128.2, 127.2, 126.7, 124.7, 119.7, 74.1, 64.3, 57.7, 51.5, 37.4 ppm. HRMS (ESI): m/z calcd for C₂₇H₂₁N₂O₃S [M + H]⁺ 453.1276, found 453.1272.

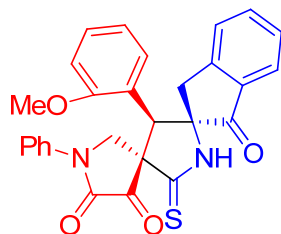


(2R,3'R,4'S)-3'-(2-Fluorophenyl)-1''-phenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3H)-trione (3ba). **3ba** was obtained as a white solid (40.9 mg, 87% yield), m.p. 158–160 °C. HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 90:10, flow rate 1.0 mL/min, detection at 254 nm): $t_R = 54.7$ min (major), $t_R = 68.0$ min (minor); 94% *ee*. $[\alpha]_D^{20} = -199.8$ (c 0.40, CH₂Cl₂): ¹H NMR (400 MHz, CDCl₃): δ 8.60 (s, 1H, NH), 7.82 (d, $J = 8.0$ Hz, 2H, ArH), 7.76 (d, $J = 7.6$ Hz, 1H, ArH), 7.57 (t, $J = 7.6$ Hz, 1H, ArH), 7.45 (t, $J = 8.0$ Hz, 2H, ArH), 7.38–7.29 (m, 3H, ArH), 7.19–7.14 (m, 1H, ArH), 7.10–6.99 (m, 2H, ArH), 6.84–6.79 (m, 1H, ArH), 4.93 (d, $J = 10.4$ Hz, 1H, NCH₂), 4.69 (s, 1H, CH), 3.99 (d, $J = 10.8$ Hz, 1H, NCH₂), 3.83 (d, $J = 18.4$ Hz, 1H, CH₂), 3.60 (d, $J = 18.0$ Hz, 1H, CH₂) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 201.4, 198.7, 195.3, 160.9 (¹ $J_{C-F} = 246.6$ Hz), 155.9, 151.1, 138.1, 136.8, 133.7, 130.7 (³ $J_{C-F} = 8.9$ Hz), 129.5 (⁴ $J_{C-F} = 2.2$ Hz), 129.3, 128.3, 127.2, 126.5, 124.91, 124.87, 124.86, 119.7, 116.2 (² $J_{C-F} = 23.1$ Hz), 73.9, 64.1, 51.7, 49.5, 37.5 ppm. HRMS (ESI): m/z calcd for C₂₇H₂₀FN₂O₃S [M + H]⁺ 471.1173, found 471.1176.



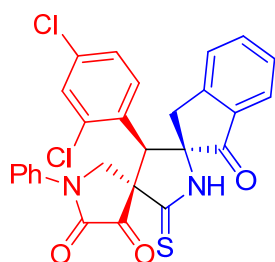
(2R,3'S,4'S)-3'-(2-Chlorophenyl)-1''-phenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3H)-trione (3ca). **3ca** was obtained as a white solid (40.1 mg, 83% yield), m.p. 148–150 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 80:20, flow rate 1.0 mL/min, detection at 254 nm): major diastereoisomer, $t_R = 46.8$ min (minor), $t_R = 38.5$ min (major); minor diastereoisomer, $t_R = 38.5$ min (major), $t_R = 13.3$ min (minor); 13:1 dr, 94% *ee* for the major diastereoisomer. $[\alpha]_D^{20} = -23.9$ (c 0.24, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 9.10 (s, 1H, NH), 7.77 (d, $J = 8.0$ Hz, 2H, ArH), 7.71 (d, $J = 7.6$ Hz, 1H, ArH), 7.53–7.39 (m, 4H, ArH), 7.33–7.23 (m, 3H, ArH), 7.20–7.07 (m, 3H, ArH), 5.10 (s, 1H, CH), 4.98 (d, $J = 11.2$ Hz, 1H, NCH₂),

4.01 (d, $J = 16.8$ Hz, 1H, CH₂), 3.97 (d, $J = 10.4$ Hz, 1H, NCH₂), 3.61 (d, $J = 18.0$ Hz, 1H, CH₂) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 202.0, 199.5, 196.2, 155.6, 150.6, 138.0, 136.7, 136.0, 133.6, 130.5, 130.3, 130.1, 129.3, 128.8, 128.2, 127.4, 127.2, 126.2, 124.8, 119.6, 74.6, 65.3, 52.25, 52.18, 37.0 ppm. HRMS (ESI): m/z calcd for C₂₇H₂₀ClN₂O₃S [M + H]⁺ 487.0878, found 487.0872.



3da

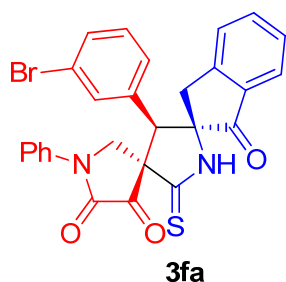
(2*R*,3'*R*,4'*S*)-3'-(2-Methoxyphenyl)-1''-phenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3*H*)-trione (3da). 3da was obtained as a light yellow solid (38.6 mg, 80% yield), m.p. 167–169 °C. HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 85:15, flow rate 1.0 mL/min, detection at 254 nm): $t_R = 41.4$ min (minor), $t_R = 30.7$ min (major), 90% *ee*. [α]_D²⁰ = –60.6 (c 0.17, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 8.47 (s, 1H, NH), 7.86–7.83 (m, 2H, ArH), 7.76 (d, $J = 7.6$ Hz, 1H, ArH), 7.54 (td, $J_1 = 1.2$ Hz, $J_2 = 7.2$ Hz, 1H, ArH), 7.45 (t, $J = 8.0$ Hz, 2H, ArH), 7.37–7.25 (m, 3H, ArH), 7.16–7.12 (m, 1H, ArH), 6.81–6.78 (m, 2H, ArH), 6.56 (d, $J = 8.0$ Hz, 1H, ArH), 4.88 (d, $J = 10.4$ Hz, 1H, NCH₂), 4.64 (s, 1H, CH), 4.00 (d, $J = 10.8$ Hz, 1H, NCH₂), 3.64 (d, $J = 18.4$ Hz, 1H, CH₂), 3.49 (d, $J = 18.4$ Hz, 1H, CH₂), 3.34 (s, 3H, OCH₃) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 201.8, 199.0, 194.9, 157.2, 156.4, 151.0, 138.3, 136.2, 134.3, 129.9, 129.3, 129.1, 127.9, 127.0, 126.5, 124.1, 120.9, 120.1, 119.8, 110.5, 73.9, 64.0, 54.1, 51.9, 51.5, 37.6 ppm; HRMS (ESI): m/z calcd for C₂₈H₂₃N₂O₄S [M + H]⁺ 483.1373, found 483.1369.



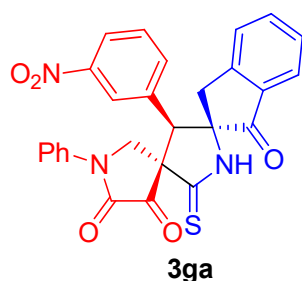
3ea

(2*R*,3'*S*,4'*S*)-3'-(2,4-Dichlorophenyl)-1''-phenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3*H*)-trione (3ea). 3ea was obtained as a yellow solid (39.0 mg, 75% yield), m.p. 153–155 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): $t_R = 7.6$ min (minor), $t_R = 25.1$ min (major); 89% *ee*. [α]_D²⁰ = –235.3 (c 0.34, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 9.17 (s, 1H, NH), 7.78 (d, $J = 8.0$ Hz, 2H, ArH), 7.71 (d, $J = 7.6$ Hz, 1H, ArH), 7.56 (t, $J = 7.4$ Hz, 1H, ArH), 7.44–7.41 (m, 3H, ArH), 7.36–7.27 (m, 3H, ArH), 7.19–7.17 (m, 2H, ArH), 5.04 (s, 1H, CH), 4.96 (d, $J = 11.2$ Hz, 1H, NCH₂), 3.97 (d, $J = 10.4$ Hz, 1H, NCH₂), 3.94 (d, $J = 17.2$ Hz, 1H, CH₂), 3.62 (d, $J = 18.0$ Hz, 1H, CH₂), ppm; ¹³C NMR (100 MHz, CDCl₃): δ 201.7, 199.4, 196.1, 155.5, 150.5, 138.0, 137.0, 136.7, 135.7, 133.4, 131.1,

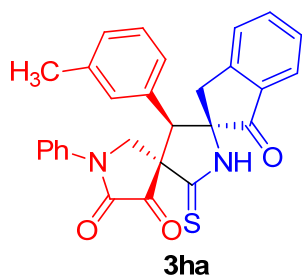
130.3, 129.3, 128.5, 127.8, 127.5, 127.3, 126.3, 124.9, 119.6, 74.5, 65.3, 52.3, 51.6, 37.0 ppm. HRMS (ESI): m/z calcd for $C_{27}H_{19}Cl_2N_2O_3S$ [$M + H$]⁺ 521.0488, found 521.0488;



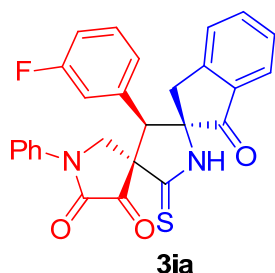
(2R,3'R,4'S)-3'-(3-Bromophenyl)-1''-phenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3H)-trione (3fa). **3fa** was obtained as a light yellow solid (37.6 mg, 71% yield), m.p. 165–168 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 65:35, flow rate 1.0 mL/min, detection at 254 nm): t_R = 7.6 min (minor), t_R = 11.1 min (major); 83% *ee*. $[\alpha]_D^{20}$ = –23.8 (*c* 0.14, CH_2Cl_2). ¹H NMR (400 MHz, $CDCl_3$): δ 9.14 (s, 1H, NH), 7.78 (d, J = 7.6 Hz, 2H, ArH), 7.70 (d, J = 7.6 Hz, 1H, ArH), 7.60 (t, J = 7.2 Hz, 1H, ArH), 7.45–7.26 (m, 6H, ArH), 7.09–6.97 (m, 3H, ArH), 4.90 (d, J = 10.8 Hz, 1H, NCH₂), 4.35 (s, 1H, CH), 3.98 (d, J = 10.8 Hz, 1H, NCH₂), 3.85 (d, J = 18.4 Hz, 1H, CH₂), 3.67 (d, J = 18.4 Hz, 1H, CH₂), ppm; ¹³C NMR (100 MHz, $CDCl_3$): δ 201.7, 198.8, 195.5, 155.7, 151.9, 138.0, 137.2, 133.7, 133.2, 132.9, 132.2, 130.8, 129.3, 128.4, 127.4, 127.3, 126.8, 124.8, 123.3, 119.7, 74.2, 64.3, 56.8, 51.4, 37.5 ppm. HRMS (ESI): m/z calcd for $C_{27}H_{20}^{79}BrN_2O_3S$ [$M + H$]⁺ 531.0373, found 531.0385; calcd for $C_{27}H_{20}^{81}BrN_2O_3S$ [$M + H$]⁺ 533.0353, found 533.0366.



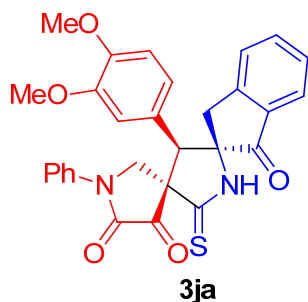
(2R,3'R,4'S)-3'-(3-Nitrophenyl)-1''-phenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3H)-trione (3ga). **3ga** was obtained as a light yellow solid (29.9 mg, 60% yield), m.p. 169–171 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 13.0 min (minor), t_R = 18.5 min (major); 77% *ee*. $[\alpha]_D^{20}$ = –55.0 (*c* 0.18, CH_2Cl_2). ¹H NMR (400 MHz, $CDCl_3$): δ 8.80 (s, 1H, NH), 8.07–8.04 (m, 1H, ArH), 7.83–7.74 (m, 4H, ArH), 7.63–7.59 (m, 1H, ArH), 7.46–7.30 (m, 7H, ArH), 4.94 (d, J = 10.8 Hz, 1H, NCH₂), 4.51 (s, 1H, CH), 4.02 (d, J = 11.2 Hz, 1H, NCH₂), 3.82 (d, J = 18.4 Hz, 1H, CH₂), 3.71 (d, J = 18.8 Hz, 1H, CH₂) ppm; ¹³C NMR (100 MHz, $CDCl_3$): δ 201.3, 198.4, 195.3, 155.6, 151.5, 148.4, 137.9, 137.5, 134.5, 133.6, 133.2, 130.6, 129.4, 128.7, 127.4, 126.7, 125.1, 124.9, 124.0, 119.7, 74.0, 64.4, 56.5, 51.6, 37.5 ppm. HRMS (ESI): m/z calcd for $C_{27}H_{20}N_3O_5S$ [$M + H$]⁺ 498.1118, found 498.1119.



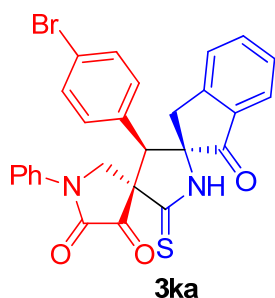
(2*R*,3'*R*,4'*S*)-1''-Phenyl-5'-thioxo-3'-(*m*-tolyl)dispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3*H*)-trione (3ha). **3ha** was obtained as a light yellow solid (43.3 mg, 93% yield), m.p. 154–156 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 8.2 min (minor), t_R = 12.0 min (major); 91% *ee*. $[\alpha]_D^{20}$ = –111.1 (*c* 0.64, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 9.16 (s, 1H, NH), 7.78 (d, *J* = 8.0 Hz, 2H, ArH), 7.69 (d, *J* = 7.6 Hz, 1H, ArH), 7.58 (t, *J* = 7.6 Hz, 1H, ArH), 7.44–7.26 (m, 5H, ArH), 7.04 (t, *J* = 7.6 Hz, 1H, ArH), 6.96 (d, *J* = 7.6 Hz, 1H, ArH), 6.77 (d, *J* = 8.0 Hz, 1H, ArH), 6.71 (s, 1H, ArH), 4.91 (d, *J* = 10.8 Hz, 1H, NCH₂), 4.38 (s, 1H, CH), 3.99 (d, *J* = 10.8 Hz, 1H, NCH₂), 3.86 (d, *J* = 18.4 Hz, 1H, CH₂), 3.66 (d, *J* = 18.8 Hz, 1H, CH₂), 2.12 (s, 3H, CH₃) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 202.2, 199.3, 195.8, 155.9, 152.3, 139.1, 138.2, 137.0, 133.9, 130.7, 130.2, 129.7, 129.2, 129.1, 128.1, 127.1, 126.7, 126.0, 124.6, 119.6, 74.2, 64.3, 57.8, 51.5, 37.4, 21.2 ppm. HRMS (ESI): *m/z* calcd for C₂₈H₂₃N₂O₃S [M + H]⁺ 467.1424, found 467.1422.



(2*R*,3'*R*,4'*S*)-3'-(3-Fluorophenyl)-1''-phenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3*H*)-trione (3ia). **3ia** was obtained as a white solid (35.3 mg, 75% yield), m.p. 225–227 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 9.2 min (minor), t_R = 14.5 min (major); 89% *ee*. $[\alpha]_D^{20}$ = –57.3 (*c* 0.4, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 8.90 (s, 1H, NH), 7.80 (d, *J* = 8.0 Hz, 2H, ArH), 7.71 (d, *J* = 8.0 Hz, 1H, ArH), 7.61 (t, *J* = 7.2 Hz, 1H, ArH), 7.46–7.28 (m, 5H, ArH), 7.19–7.13 (m, 1H, ArH), 6.89 (td, *J*₁ = 8.4 Hz, *J*₂ = 2.0 Hz, 1H, ArH), 6.78 (d, *J* = 7.6 Hz, 1H, ArH), 6.70–6.67 (m, 1H, ArH), 4.91 (d, *J* = 10.8 Hz, 1H, NCH₂), 4.40 (s, 1H, CH), 3.99 (d, *J* = 10.8 Hz, 1H, NCH₂), 3.87 (d, *J* = 18.4 Hz, 1H, CH₂), 3.68 (d, *J* = 18.8 Hz, 1H, CH₂) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 201.7, 198.8, 195.5, 162.7 (¹*J*_{C-F} = 247.7 Hz), 155.7, 152.0, 138.1, 137.2, 133.7, 133.3 (³*J*_{C-F} = 7.1 Hz), 133.2, 131.0 (³*J*_{C-F} = 8.3 Hz), 129.3, 128.4, 127.3, 126.8, 124.84, 124.79, 119.7, 116.7 (²*J*_{C-F} = 22.4 Hz), 116.2 (²*J*_{C-F} = 20.8 Hz), 74.0, 64.3, 56.8, 51.4, 37.5 ppm. HRMS (ESI): *m/z* calcd for C₂₇H₂₀FN₂O₃S [M + H]⁺ 471.1173, found 471.1181.

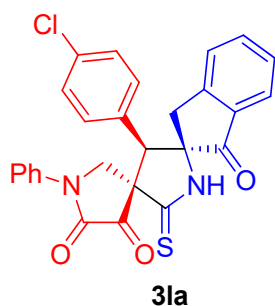


(2R,3'R,4'S)-3'-(3,4-Dimethoxyphenyl)-1''-phenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3H)-trione (3ja). **3ja** was obtained as a light yellow solid (41.5 mg, 81% yield), m.p. 152–154 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 65:35, flow rate 1.0 mL/min, detection at 254 nm): t_R = 8.7 min (minor), t_R = 17.3 min (major); 91% *ee*. $[\alpha]_D^{20}$ = –111.3 (*c* 0.68, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 9.15 (s, 1H, NH), 7.79 (d, *J* = 8.0 Hz, 2H, ArH), 7.68 (d, *J* = 8.0 Hz, 1H, ArH), 7.57 (t, *J* = 7.6 Hz, 1H, ArH), 7.43 (t, *J* = 7.8 Hz, 2H, ArH), 7.37–7.27 (m, 3H, ArH), 6.60 (d, *J* = 8.4 Hz, 1H, ArH), 6.48 (dd, *J*₁ = 2.0 Hz, *J*₂ = 8.4 Hz, 1H, ArH), 6.33 (d, *J* = 2.0 Hz, 1H, ArH), 4.94 (d, *J* = 10.8 Hz, 1H, NCH₂), 4.35 (s, 1H, CH), 4.00 (d, *J* = 10.8 Hz, 1H, NCH₂), 3.85 (d, *J* = 18.4 Hz, 1H, CH₂), 3.72 (s, 3H, OCH₃), 3.64 (d, *J* = 18.4 Hz, 1H, CH₂), 3.56 (s, 3H, OCH₃) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 202.6, 199.2, 196.1, 155.9, 152.4, 149.1, 149.0, 138.1, 137.0, 133.9, 129.3, 128.2, 127.2, 126.8, 124.5, 122.9, 121.5, 119.6, 111.8, 111.3, 74.1, 64.2, 58.0, 55.7, 55.6, 51.5, 37.4 ppm. HRMS (ESI): *m/z* calcd for C₂₉H₂₅N₂O₅S [M + H]⁺ 513.1479, found 513.1478.

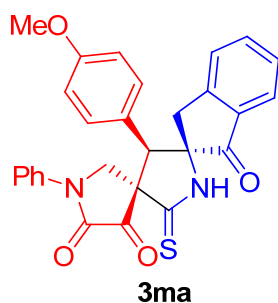


(2R,3'R,4'S)-3'-(4-Bromophenyl)-1''-phenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3H)-trione (3ka). **3ka** was obtained as a white solid (45.0 mg, 85% yield), m.p. 165–167 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 12.4 min (minor), t_R = 28.9 min (major); 80% *ee*. $[\alpha]_D^{20}$ = –70.8 (*c* 0.48, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 9.08 (s, 1H, NH), 7.78 (d, *J* = 7.6, 2H, ArH), 7.68 (d, *J* = 8.0 Hz, 1H, ArH), 7.61 (t, *J* = 7.2 Hz, 1H, ArH), 7.45–7.27 (m, 7H, ArH), 6.85 (d, *J* = 8.8 Hz, 2H, ArH), 4.91 (d, *J* = 10.8 Hz, 1H, NCH₂), 4.37 (s, 1H, CH), 3.96 (d, *J* = 10.8 Hz, 1H, NCH₂), 3.82 (d, *J* = 18.4 Hz, 1H, CH₂), 3.67 (d, *J* = 18.4 Hz, 1H, CH₂), ppm; ¹³C NMR (100 MHz, CDCl₃): δ 201.9, 198.8, 195.7, 155.7, 152.0, 138.0, 137.3, 133.7, 132.5, 130.9, 129.9, 129.3, 128.4, 127.3, 126.8, 124.7, 123.4, 119.6, 74.0, 64.3, 56.9, 51.4, 37.4 ppm. HRMS (ESI): *m/z* calcd for C₂₇H₂₀⁷⁹BrN₂O₃S [M + H]⁺ 531.0373, found 531.0375; calcd for C₂₇H₂₀⁸¹BrN₂O₃S [M + H]⁺

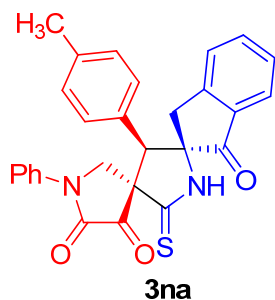
533.0353, found 533.0359.



(2R,3'R,4'S)-3'-(4-Chlorophenyl)-1''-phenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3H)-trione (3la). 3la was obtained as a light yellow solid (44.2 mg, 91% yield), m.p. 157–159 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): $t_R = 11.8$ min (minor), $t_R = 27.2$ min (major); 89% *ee*. $[\alpha]_D^{20} = -92.4$ (*c* 0.6, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 9.14 (s, 1H, NH), 7.78 (d, *J* = 8.0, 1H, ArH), 7.67 (d, *J* = 7.6 Hz, 1H, ArH), 7.60 (t, *J* = 8.0 Hz, 1H, ArH), 7.45–7.28 (m, 6H, ArH), 7.13 (d, *J* = 8.4 Hz, 2H, ArH), 6.92 (d, *J* = 8.8 Hz, 2H, ArH), 4.91 (d, *J* = 10.8 Hz, 1H, NCH₂), 4.38 (s, 1H, CH), 3.96 (d, *J* = 10.8 Hz, 1H, NCH₂), 3.83 (d, *J* = 18.4 Hz, 1H, CH₂), 3.66 (d, *J* = 18.4 Hz, 1H, CH₂) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 202.0, 198.8, 195.7, 155.7, 152.0, 138.0, 137.2, 135.2, 133.7, 130.6, 129.5, 129.3, 128.3, 127.3, 126.8, 124.7, 119.6, 74.1, 64.3, 56.9, 51.4, 37.4 ppm. HRMS (ESI): *m/z* calcd for C₂₇H₂₀ClN₂O₃S [M + H]⁺ 487.0878, found 487.0870.

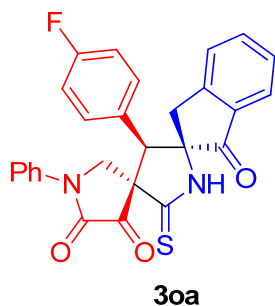


(2R,3'R,4'S)-3'-(4-Methoxyphenyl)-1''-phenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3H)-trione (3ma). 3ma was obtained as a white solid (46.3 mg, 96% yield), m.p. 161–163 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): $t_R = 10.7$ min (minor), $t_R = 27.4$ min (major); 91% *ee*. $[\alpha]_D^{20} = -78.4$ (*c* 0.6, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 9.10 (s, 1H, NH), 7.77 (d, *J* = 8.0 Hz, 2H, ArH), 7.66 (d, *J* = 7.6 Hz, 1H, ArH), 7.57 (t, *J* = 7.2 Hz, 1H, ArH), 7.44–7.28 (m, 5H, ArH), 6.90 (d, *J* = 8.4 Hz, 2H, ArH), 6.65 (d, *J* = 8.4 Hz, 2H, ArH), 4.91 (d, *J* = 10.8 Hz, 1H, NCH₂), 4.34 (s, 1H, CH), 3.97 (d, *J* = 10.4 Hz, 1H, NCH₂), 3.89 (d, *J* = 18.4, 1H, CH₂), 3.65 (d, *J* = 18.0 Hz, 1H, CH₂), 3.66 (s, 3H, OCH₃) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 202.3, 199.3, 159.7, 155.8, 152.3, 138.1, 137.0, 133.8, 130.6, 129.2, 128.1, 127.1, 126.7, 124.6, 122.4, 119.6, 114.6, 74.2, 64.5, 57.4, 55.2, 51.5, 37.3 ppm. HRMS (ESI): *m/z* calcd for C₂₈H₂₃N₂O₄S [M + H]⁺ 483.1373, found 483.1371.



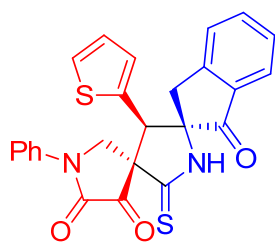
(2R,3'R,4'S)-1''-Phenyl-5'-thioxo-3'-(*p*-tolyl)dispiro[indene-2,2'-pyrrolidine-4',3''-

pyrrolidine]-1,4'',5''(3H)-trione (3na). 3na was obtained as a light yellow solid (46.5 mg, >99% yield), m.p. 167–169 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 10.6 min (minor), t_R = 20.9 min (major); 91% ee. $[\alpha]_D^{20}$ = –133.8 (c 0.6, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 9.25 (s, 1H, NH), 7.77 (d, *J* = 8.0 Hz, 2H, ArH), 7.66 (d, *J* = 7.6 Hz, 1H, ArH), 7.57 (t, *J* = 7.4 Hz, 1H, ArH), 7.43–7.28 (m, 5H, ArH), 6.93 (d, *J* = 8.0 Hz, 2H, ArH), 6.84 (d, *J* = 8.0 Hz, 2H, ArH), 4.90 (d, *J* = 10.8 Hz, 1H, NCH₂), 4.39 (s, 1H, CH), 3.98 (d, *J* = 10.4 Hz, 1H, NCH₂), 3.86 (d, *J* = 18.4 Hz, 1H, CH₂), 3.65 (d, *J* = 18.4 Hz, 1H, CH₂), 2.17 (s, 3H, CH₃) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 202.2, 199.2, 195.9, 155.9, 152.3, 138.8, 138.1, 136.9, 133.8, 129.9, 129.2, 129.1, 128.1, 127.7, 127.1, 126.7, 124.6, 119.6, 74.2, 64.4, 57.5, 51.4, 37.3, 20.8 ppm. HRMS (ESI): *m/z* calcd for C₂₈H₂₃N₂O₃S [M + H]⁺ 467.1424, found 467.1415.



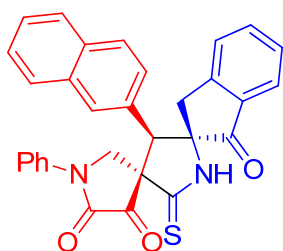
(2R,3'R,4'S)-3'-(4-Fluorophenyl)-1''-phenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-

pyrrolidine]-1,4'',5''(3H)-trione (3oa). 3oa was obtained as a light yellow solid (38.1 mg, 81% yield), m.p. 154–156 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 10.8 min (minor), t_R = 22.2 min (major); 86% ee. $[\alpha]_D^{20}$ = –22.9 (c 0.34, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 8.99 (s, 1H, NH), 7.78 (d, *J* = 8.0 Hz, 2H, ArH), 7.69 (d, *J* = 7.6 Hz, 1H, ArH), 7.60 (t, *J* = 7.4 Hz, 1H, ArH), 7.45–7.28 (m, 5H, ArH), 6.99–6.96 (m, 2H, ArH), 6.84 (t, *J* = 8.4 Hz, 2H, ArH), 4.92 (d, *J* = 10.8 Hz, 1H, NCH₂), 4.37 (s, 1H, CH), 3.96 (d, *J* = 10.4 Hz, 1H, NCH₂), 3.86 (d, *J* = 18.4 Hz, 1H, CH₂), 3.67 (d, *J* = 18.4 Hz, 1H, CH₂) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 202.0, 199.0, 195.8, 162.7 (¹*J*_{C-F} = 248.6 Hz), 155.7, 152.0, 138.1, 137.2, 133.7, 131.2 (³*J*_{C-F} = 8.2 Hz), 129.3, 128.3, 127.3, 126.7, 126.6 (⁴*J*_{C-F} = 3.3 Hz), 124.7, 119.6, 116.4 (²*J*_{C-F} = 21.4 Hz), 74.2, 64.4, 57.0, 51.5, 37.3 ppm. HRMS (ESI): *m/z* calcd for C₂₇H₂₀FN₂O₃S [M + H]⁺ 471.1173, found 471.1165.



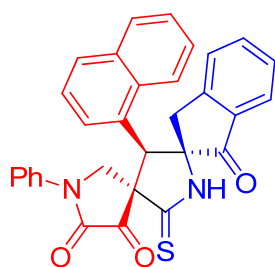
3pa

(2R,3'R,4'S)-1''-Phenyl-3'-(thiophen-2-yl)-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3H)-trione (3pa). **3pa** was obtained as a white solid (32.5 mg, 71% yield), m.p. 250–252 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 60:40, flow rate 1.0 mL/min, detection at 254 nm): t_R = 12.6 min (major), t_R = 21.3 min (minor); >99% *ee*. $[\alpha]_D^{20}$ = –26.1 (*c* 0.22, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 8.90 (s, 1H, NH), 7.80 (d, *J* = 8.0 Hz, 2H, ArH), 7.70 (d, *J* = 7.6 Hz, 1H, ArH), 7.62 (t, *J* = 7.4 Hz, 1H, ArH), 7.46–7.28 (m, 5H, ArH), 7.09 (d, *J* = 4.8 Hz, 1H, ArH), 6.78 (t, *J* = 4.4 Hz, 1H, ArH), 6.71 (d, *J* = 3.3 Hz, 1H, ArH), 4.95 (d, *J* = 10.8 Hz, 1H, NCH₂), 4.63 (s, 1H, CH), 4.10 (d, *J* = 18.4 Hz, 1H, CH₂), 4.03 (d, *J* = 10.8 Hz, 1H, NCH₂), 3.66 (d, *J* = 18.4 Hz, 1H, CH₂) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 201.9, 198.6, 195.0, 155.6, 152.3, 138.1, 137.1, 133.8, 131.9, 129.3, 129.0, 128.3, 127.5, 127.2, 126.8, 124.8, 119.6, 74.0, 64.5, 53.2, 51.5, 38.0 ppm. HRMS (ESI): *m/z* calcd for C₂₅H₁₉N₂O₃S₂ [M + H]⁺ 459.0832, found 459.0854;



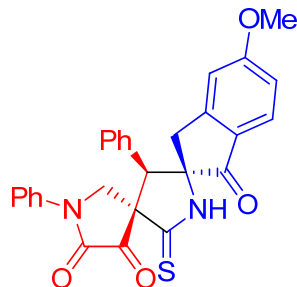
3qa

(2R,3'R,4'S)-3'-(Naphthalen-2-yl)-1''-phenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3H)-trione (3qa). **3qa** was obtained as a light yellow solid (46.2 mg, 92% yield), m.p. 165–167 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/ethyl acetate = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 10.8 min (minor), t_R = 19.3 min (major); 94% *ee*. $[\alpha]_D^{20}$ = –68.6 (*c* 0.8, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 9.22 (s, 1H, NH), 7.75 (d, *J* = 8.0 Hz, 2H, ArH), 7.69–7.62 (m, 4H, ArH), 7.52–7.36 (m, 6H, ArH), 7.32–7.23 (m, 3H, ArH), 7.06 (d, *J* = 8.4 Hz, 1H, ArH), 4.94 (d, *J* = 10.8 Hz, 1H, NCH₂), 4.63 (s, 1H, CH), 4.05 (d, *J* = 10.8 Hz, 1H, NCH₂), 3.93 (d, *J* = 18.4 Hz, 1H, CH₂), 3.73 (d, *J* = 18.4 Hz, 1H, CH₂) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 202.1, 199.2, 195.9, 155.9, 152.3, 138.1, 137.0, 133.7, 132.9, 132.8, 129.22, 129.17, 128.3, 128.2, 128.0, 127.4, 127.1, 126.9, 126.82, 126.76, 126.0, 124.7, 119.6, 74.3, 64.5, 57.8, 51.5, 37.5 ppm. HRMS (ESI): *m/z* calcd for C₃₁H₂₃N₂O₃S [M + H]⁺ 503.1424, found 503.1426;



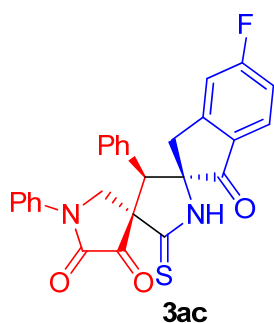
3ra

(2R,3'R,4'S)-3'-(Naphthalen-1-yl)-1''-phenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3H)-trione (3ra). 3ra was obtained as a white solid (30.1 mg, 60% yield), m.p. 222–224 °C. HPLC (Daicel Chiralpak IC, *n*-hexane/2-propanol = 65:35, flow rate 1.0 mL/min, detection at 254 nm): t_R = 15.8 min (major), t_R = 40.5 min (minor); 75 % *ee*. $[\alpha]_D^{20}$ = –92.0 (*c* 0.58, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 9.72 (s, 1H, NH), 8.16 (d, *J* = 8.4 Hz, 1H, ArH), 7.70–7.63 (m, 4H, ArH), 7.55–7.49 (m, 2H, ArH), 7.40–7.29 (m, 6H, ArH), 7.22–7.15 (m, 2H, ArH), 7.02 (t, *J* = 7.4 Hz, 1H, ArH), 5.55 (s, 1H, CH), 5.06 (d, *J* = 10.8 Hz, 1H, NCH₂), 4.19 (d, *J* = 18.0 Hz, 1H, CH₂), 3.86 (d, *J* = 10.8 Hz, 1H, NCH₂), 3.72 (d, *J* = 17.6 Hz, 1H, CH₂) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 203.5, 200.2, 197.1, 155.9, 151.2, 138.0, 136.7, 133.9, 133.8, 132.8, 129.8, 129.2, 129.0, 127.8, 127.3, 127.1, 127.0, 126.8, 126.1, 124.8, 124.4, 122.4, 119.5, 74.9, 65.4, 51.8, 51.5, 37.6 ppm. HRMS (ESI): *m/z* calcd for C₃₁H₂₃N₂O₃S [M + H]⁺ 503.1424, found 503.1419;

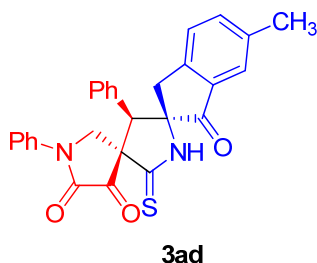


3ab

(2R,3'R,4'S)-5-methoxy-1'',3'-diphenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3H)-trione (3ab). 3ab was obtained as a white solid (43.9 mg, 91% yield), m.p. 160–162 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 65:35, flow rate 1.0 mL/min, detection at 254 nm): t_R = 9.6 min (minor), t_R = 22.3 min (major); 93% *ee*. $[\alpha]_D^{20}$ = –99.5 (*c* 0.7, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 9.33 (s, 1H, NH), 7.79 (d, *J* = 7.6 Hz, 2H, ArH), 7.58 (d, *J* = 8.4 Hz, 1H, ArH), 7.42 (t, *J* = 8.0 Hz, 2H, ArH), 7.28 (t, *J* = 8.0 Hz, 1H, ArH), 7.18–7.14 (m, 3H, ArH), 6.95–6.93 (m, 2H, ArH), 6.82 (dd, *J*₁ = 2.0 Hz, *J*₂ = 8.8 Hz, 1H, ArH), 6.77 (s, 1H, ArH), 4.92 (d, *J* = 10.8 Hz, 1H, NCH₂), 4.45 (s, 1H, CH), 4.00 (d, *J* = 10.8 Hz, 1H, NCH₂), 3.83 (s, 3H, OCH₃), 3.78 (d, *J* = 18.4 Hz, 1H, CH₂), 3.61 (d, *J* = 18.4 Hz, 1H, CH₂) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 199.5, 199.0, 195.9, 167.1, 156.0, 155.8, 138.1, 131.1, 129.3, 129.2, 129.1, 128.7, 127.1, 127.0, 126.5, 119.6, 117.0, 109.2, 74.4, 64.3, 57.4, 55.8, 51.5, 37.5 ppm; HRMS (ESI): *m/z* calcd for C₂₈H₂₃N₂O₄S [M + H]⁺ 483.1373, found 483.1365.

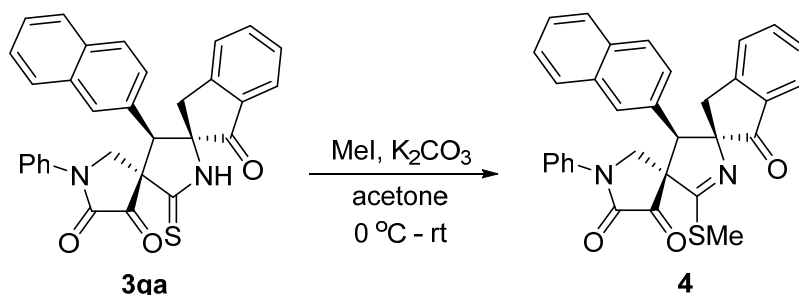


(2*R*,3'*R*,4'*S*)-5-fluoro-1'',3'-diphenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3*H*)-trione (3ac). 3ac was obtained as a light yellow solid (44.2 mg, 94% yield), m.p. 156–158 °C. HPLC (Daicel Chiralpak IB, *n*-hexane/2-propanol = 85:15, flow rate 1.0 mL/min, detection at 254 nm): t_R = 24.9 min (major), t_R = 29.6 min (minor); 88% *ee*. $[\alpha]_D^{20}$ = –55.7 (*c* 0.20, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 8.84 (s, 1H, NH), 7.79–7.73 (m, 3H, ArH), 7.44 (t, *J* = 7.8 Hz, 2H, ArH), 7.30 (t, *J* = 7.4 Hz, 1H, ArH), 7.22–7.14 (m, 3H, ArH), 7.06–7.02 (m, 2H, ArH), 6.92 (d, *J* = 6.8 Hz, 2H, ArH), 4.90 (d, *J* = 10.8 Hz, 1H, NCH₂), 4.38 (s, 1H, CH), 3.99 (d, *J* = 10.8 Hz, 1H, NCH₂), 3.85 (d, *J* = 18.4 Hz, 1H, CH₂), 3.65 (d, *J* = 18.8 Hz, 1H, CH₂) ppm; ¹³C NMR (100 MHz, DMSO-*d*₆): δ 200.7, 198.0, 196.6, 167.3 (¹*J*_{C-F} = 254.6 Hz), 155.5, 155.1 (³*J*_{C-F} = 11.0 Hz), 138.0, 131.5, 130.6, 129.2, 129.0, 128.44, 128.37, 127.0, 126.9, 119.2, 116.6 (²*J*_{C-F} = 23.9 Hz), 113.5 (²*J*_{C-F} = 22.8 Hz), 73.8, 64.5, 56.4, 51.1, 36.9 ppm; HRMS (ESI): *m/z* calcd for C₂₇H₂₀FN₂O₃S [M + H]⁺ 471.1132, found 471.1174.

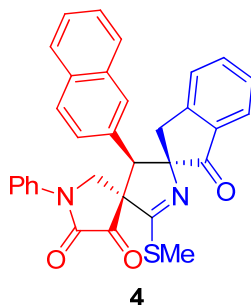


(2*R*,3'*R*,4'*S*)-6-Methyl-1'',3'-diphenyl-5'-thioxodispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5''(3*H*)-trione (3ad). 3ad was obtained as a white solid (37.3 mg, 80% yield), m.p. 159–161 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 9.5 min (minor), t_R = 14.9 min (major); 86% *ee*. $[\alpha]_D^{20}$ = –110.3 (*c* 0.5, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 9.12 (s, 1H, NH), 7.79 (d, *J* = 8.0 Hz, 2H, ArH), 7.46–7.38 (m, 4H, ArH), 7.31–7.22 (m, 2H, ArH), 7.17–7.13 (m, 3H, ArH), 6.94 (d, *J* = 6.4 Hz, 2H, ArH), 4.93 (d, *J* = 10.8 Hz, 1H, NCH₂), 4.46 (s, 1H, CH), 4.01 (d, *J* = 10.8 Hz, 1H, NCH₂), 3.80 (d, *J* = 18.4 Hz, 1H, CH₂), 3.60 (d, *J* = 18.4 Hz, 1H, CH₂), 2.32 (s, 3H, CH₃) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 202.2, 199.1, 195.7, 155.9, 149.7, 138.4, 138.3, 138.2, 134.0, 131.0, 129.3, 129.1, 128.8, 127.1, 126.4, 124.4, 119.6, 74.4, 64.3, 57.7, 51.5, 37.1, 21.0 ppm. HRMS (ESI): *m/z* calcd for C₂₈H₂₃N₂O₃S [M + H]⁺ 467.1424, found 467.1415.

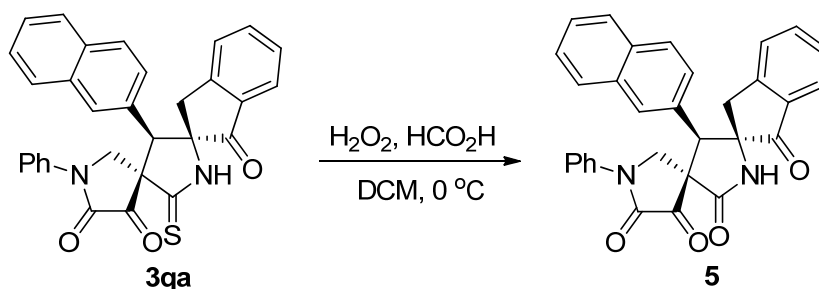
5. Produce for the synthesis of compound 4 and 5



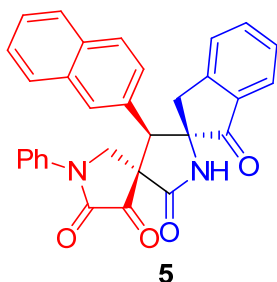
The corresponding chiral compound **3qa** (50 mg, 0.1 mmol) was dissolved in 5 mL acetone and lower the temperature to 0 °C, then potassium carbonate (1 equiv.) was added to the system. Methyl iodide (1.2 equiv.) solution in acetone was slowly added, and warm the solution to room temperature and stirred overnight. When the reaction was completed detected by TLC, the mixture was concentrated under vacuum, the crude product was purified by column chromatography (eluent: petroleum ether/ ethyl acetate = 5:1 to 2:1 v/v) to give the compound **4**.



(2R,3'R,4'S)-5'-(Methylthio)-3'-(naphthalen-2-yl)-1''-phenyl-3'H-dispiro[indene-2,2'-pyrrole-4',3''-pyrrolidine]-1,4'',5''(3H)-trione (4). **4** was obtained as a white solid (52.0 mg, >99 % yield), m.p. 273–275 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): t_R = 12.8 min (minor), t_R = 14.8 min (major); 91% *ee*. $[\alpha]_D^{20} = -38.7$ (*c* 0.31, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 7.81 (t, *J* = 8.0 Hz, 3H, ArH), 7.72–7.66 (m, 3H, ArH), 7.55 (t, *J* = 7.2, 1H, ArH), 7.47 – 7.39 (m, 5H, ArH), 7.37–7.28 (m, 3H, ArH), 7.14 (dd, *J*₁ = 1.4 Hz, *J*₂ = 8.6 Hz, 1H, ArH), 4.60 (d, *J* = 11.2 Hz, 1H, NCH₂), 4.57 (s, 1H, CH), 4.39 (d, *J* = 11.6 Hz, 1H, NCH₂), 3.54 (d, *J* = 18.0 Hz, 1H, CH₂), 3.46 (d, *J* = 18.0 Hz, 1H, CH₂), 2.45 (s, 3H, SCH₃) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 204.3, 195.5, 171.7, 156.6, 153.4, 138.0, 136.0, 134.5, 133.0, 132.7, 130.6, 129.4, 128.9, 127.9, 127.7, 127.4, 127.2, 126.7, 126.61, 126.56, 124.8, 119.5, 85.2, 66.5, 60.1, 51.4, 37.8, 13.9 ppm. HRMS (ESI): *m/z* calcd for C₃₂H₂₅N₂O₃S [M + H]⁺ 517.1580, found 517.1575.



The corresponding chiral compound **3qa** (50 mg, 0.1 mmol) was dissolved in 5 mL DCM and lower the temperature to 0 °C, H₂O₂ (0.5 mL, 30% wt%) was added slowly, after the addition, HCO₂H (0.5 ml) was also added slowly to the reaction system. Monitoring the reaction by TLC, saturated sodium bicarbonate solution was added to quench the reaction at 0 °C when the reaction completed. The aqueous phase was extracted with DCM, and the organic phase was combined. The reaction mixture was concentrated under vacuum, and the crude product was purified by column chromatography (eluent: petroleum ether/ethyl acetate = 3:1–2:1 v/v) to give the compound **5**.



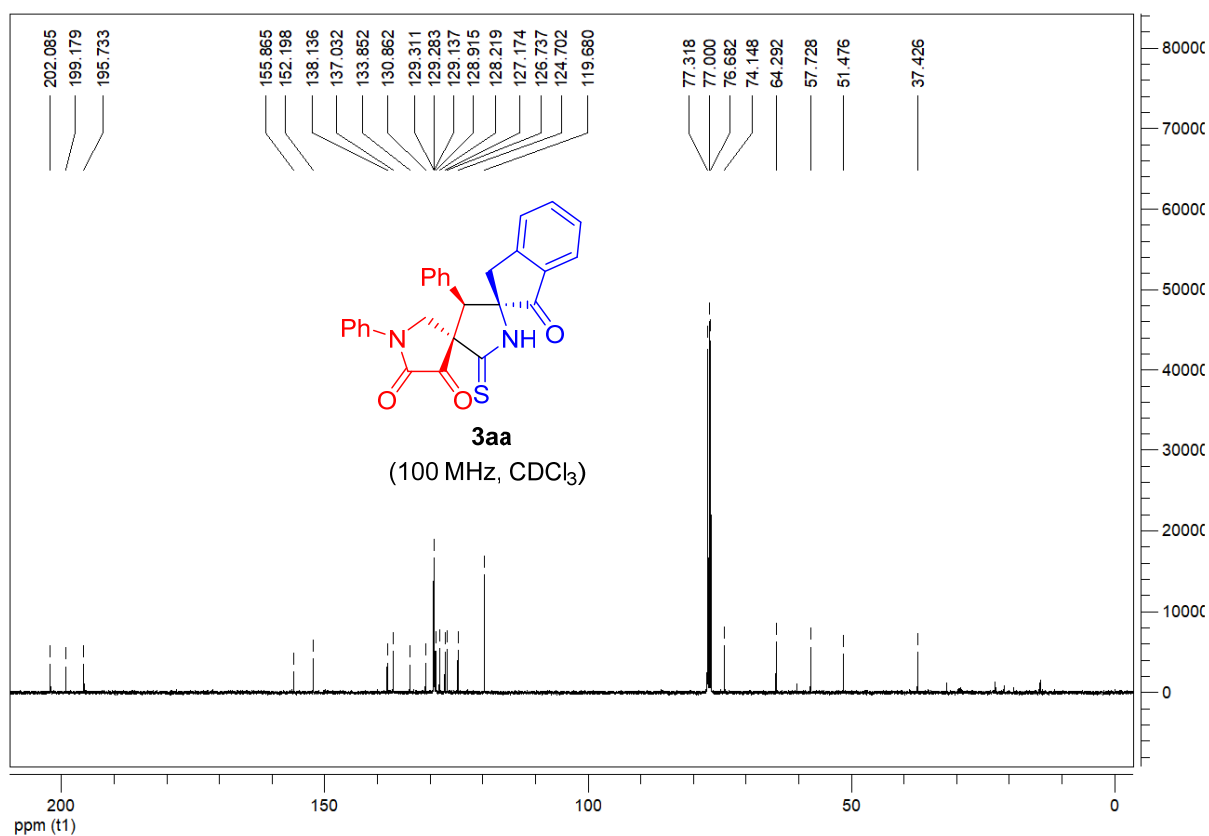
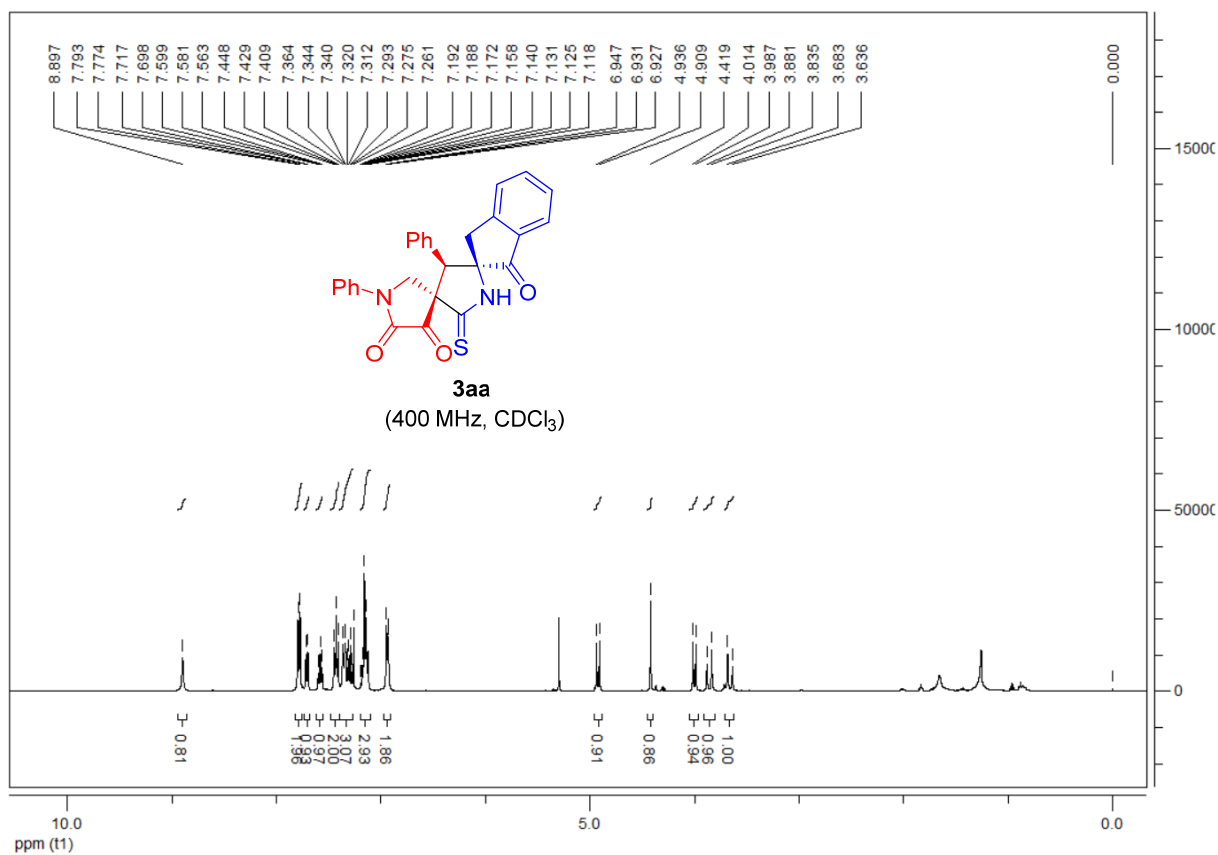
(2*R*,3'*R*,4'*S*)-3'-(naphthalen-2-yl)-1''-phenyldispiro[indene-2,2'-pyrrolidine-4',3''-pyrrolidine]-1,4'',5'',5''(3*H*)-tetraone (5).

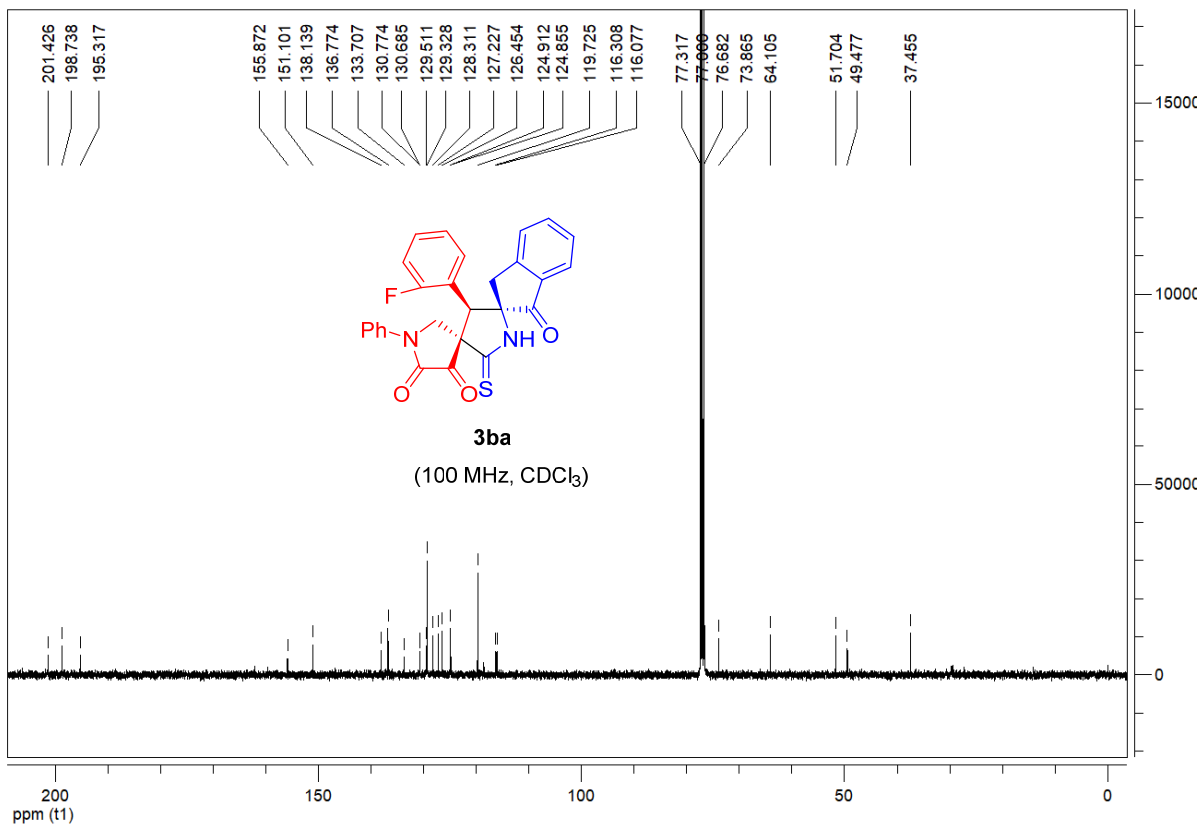
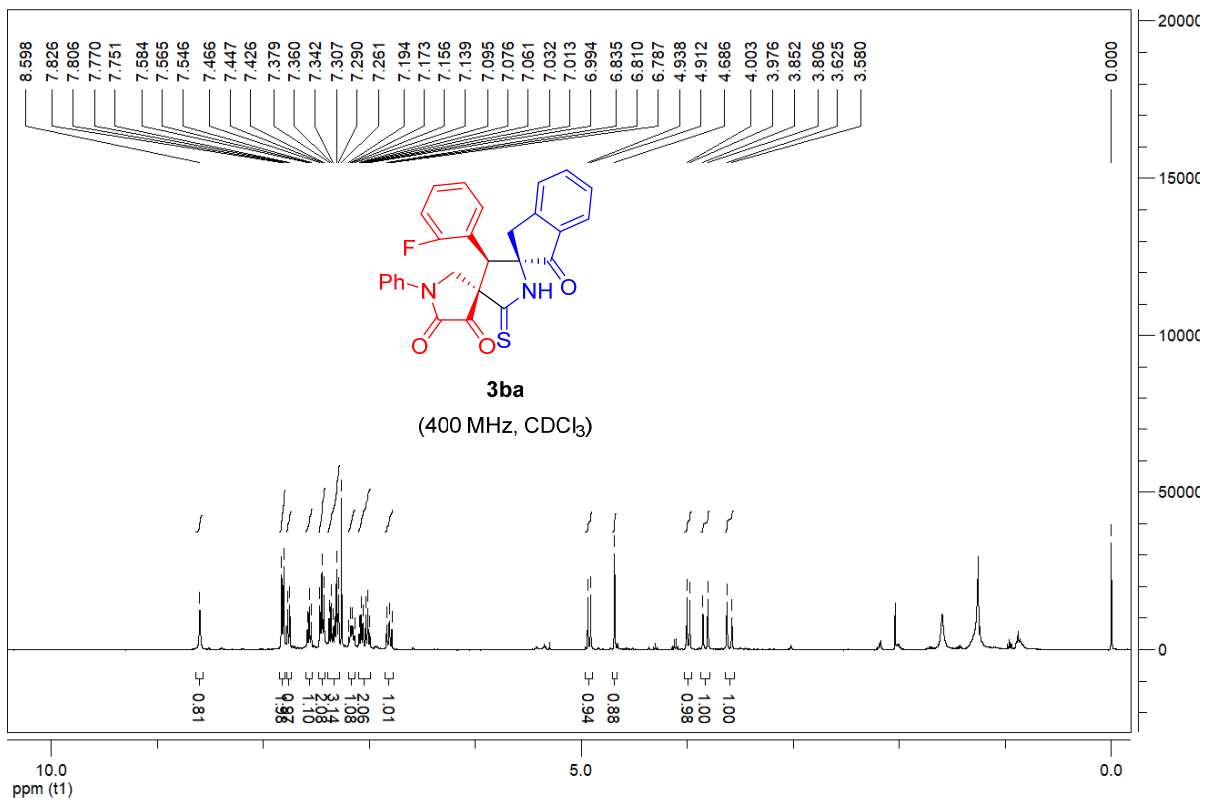
5 was obtained as a white solid (41.4 mg, 85 % yield), m.p. 189–190 °C. HPLC (Daicel Chiralpak IA, *n*-hexane/2-propanol = 70:30, flow rate 1.0 mL/min, detection at 254 nm): *t*_R = 23.4 min (minor), *t*_R = 28.0 min (major); 86% *ee*. [α]_D²⁰ = -73.0 (*c* 0.83, CH₂Cl₂). ¹H NMR (400 MHz, CDCl₃): δ 7.74 (d, *J* = 8.0 Hz, 2H, ArH), 7.70–7.63 (m, 3H, ArH), 7.58 (d, *J* = 8.4, 1H, ArH), 7.47–7.39 (m, 5H, ArH+NH), 7.35 (t, *J* = 8.0 Hz, 2H, ArH), 7.27–7.21 (m, 3H, ArH), 7.02 (dd, *J*₁ = 1.4 Hz, *J*₂ = 8.6 Hz, 1H, ArH), 4.71 (d, *J* = 10.8 Hz, 1H, NCH₂), 4.49 (s, 1H, CH), 4.01 (d, *J* = 10.8 Hz, 1H, NCH₂), 3.94 (d, *J* = 18.4 Hz, 1H, CH₂), 3.60 (d, *J* = 18.4 Hz, 1H, CH₂) ppm; ¹³C NMR (100 MHz, CDCl₃): δ 204.1, 196.9, 170.8, 156.3, 152.4, 138.1, 136.8, 134.0, 132.9, 132.8, 129.2, 129.0, 128.84, 128.77, 128.0, 127.4, 127.1, 126.8, 126.7, 126.6, 125.9, 124.4, 119.3, 68.7, 57.8, 56.9, 49.2, 38.0 ppm. HRMS (ESI): *m/z* calcd for C₃₁H₂₃N₂O₄ [M + H]⁺ 487.1652, found 487.1653.

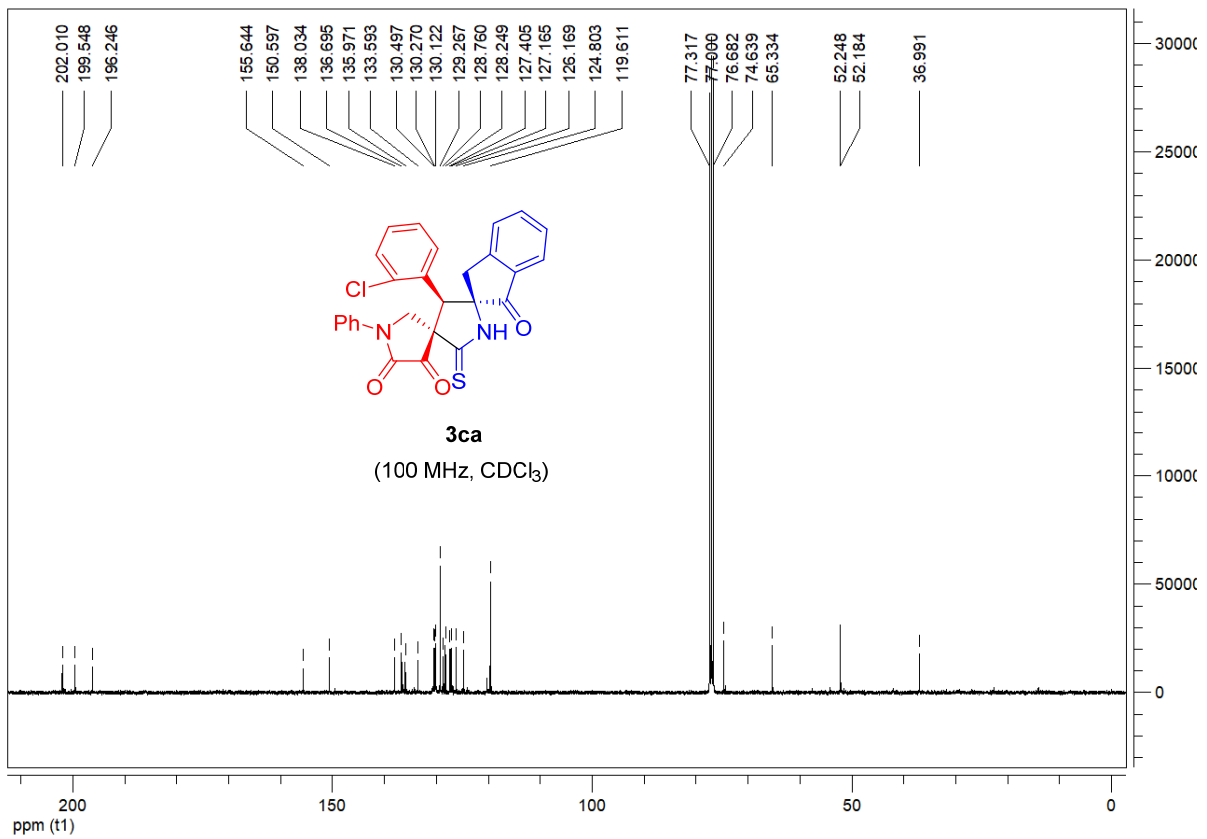
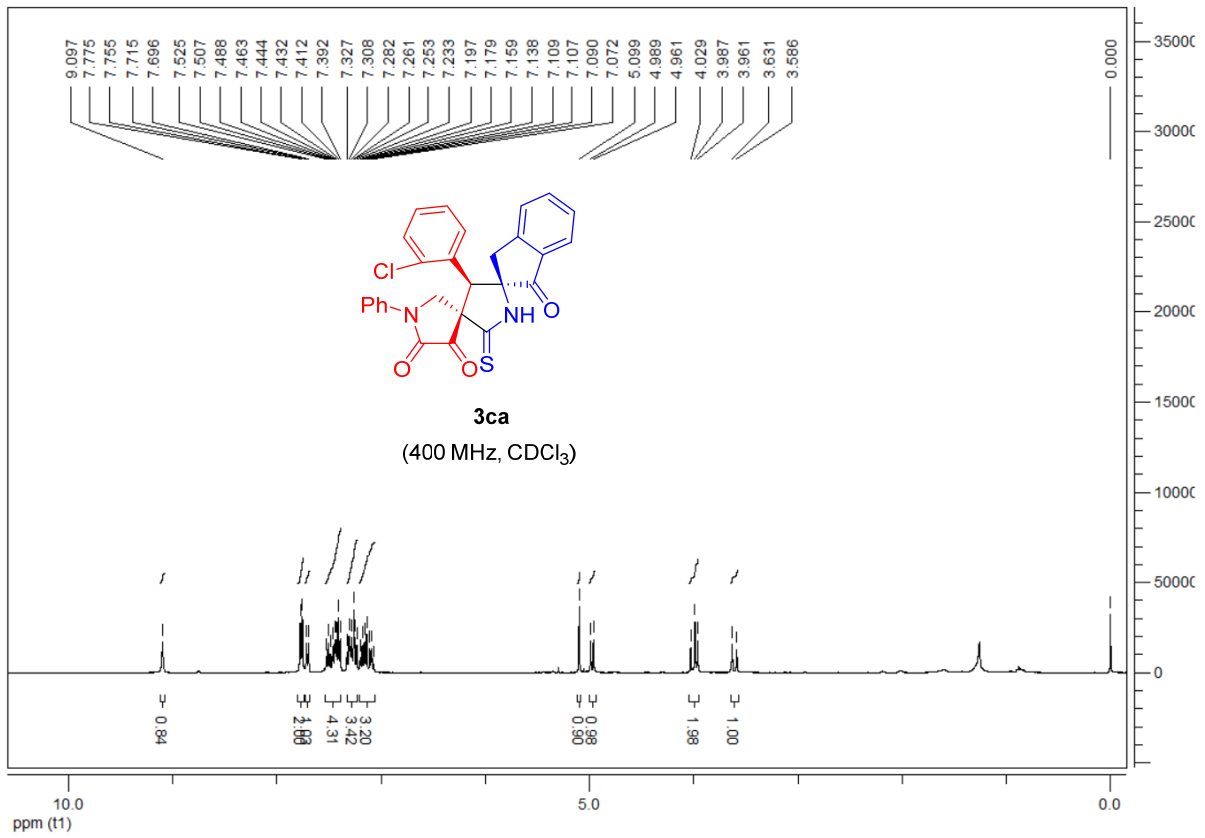
6. References

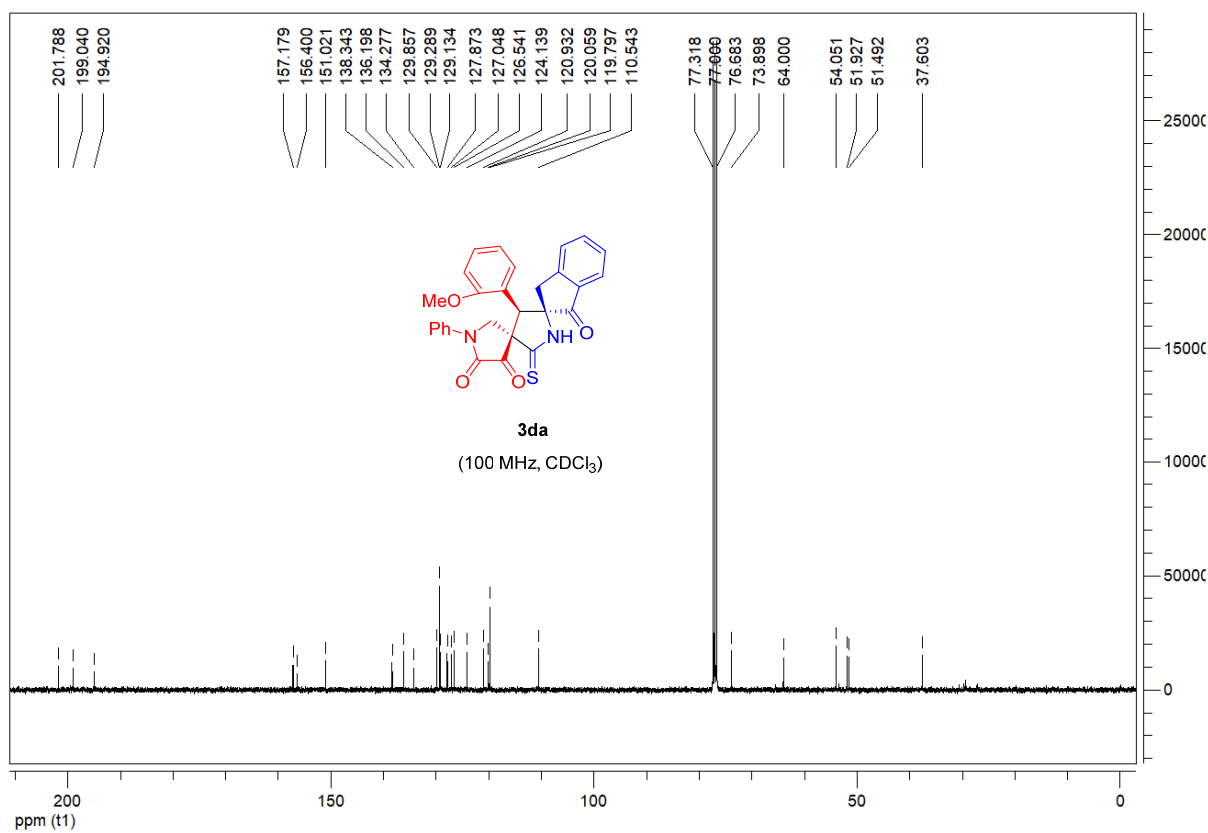
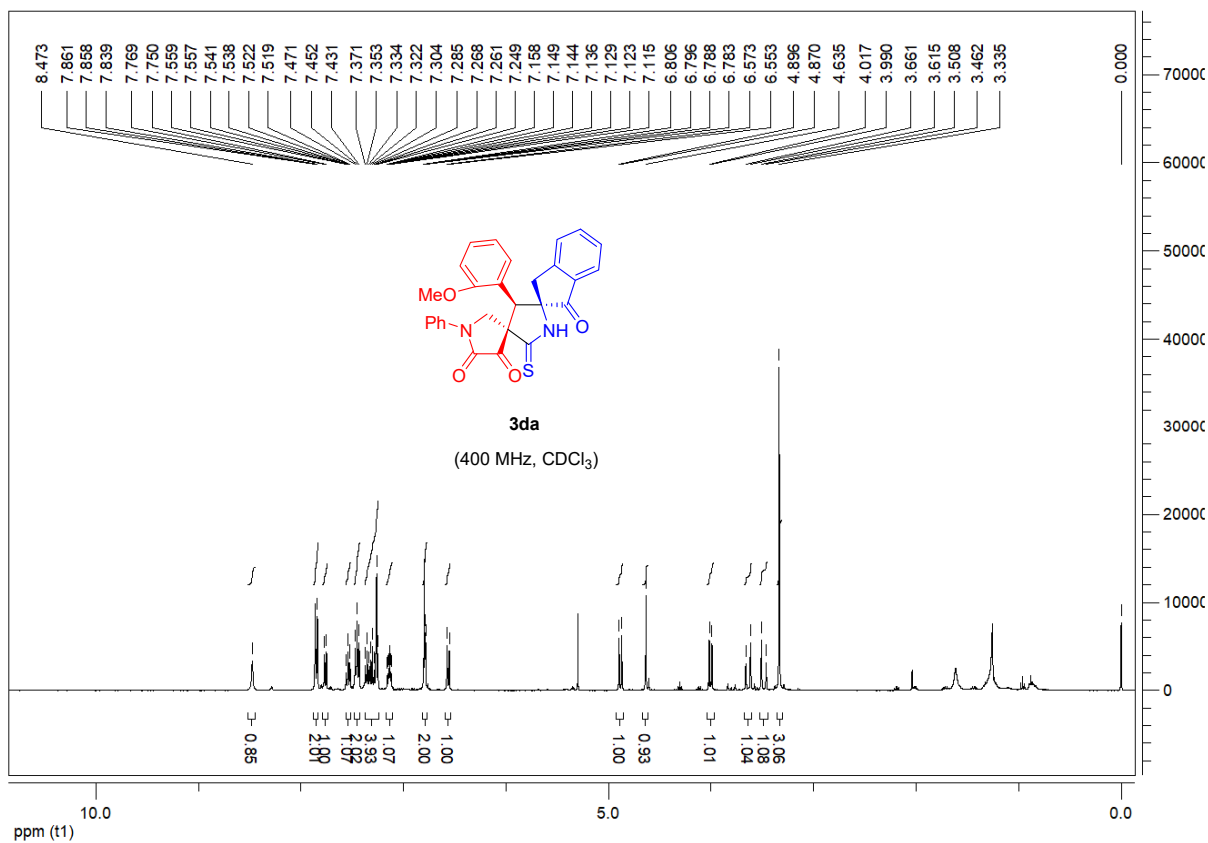
1. X. Chen, L. Zhu, L. Fang, S. Yan and J. Lin, RSC Adv. **2014**, 4, 9926.
2. Zhao, B.-L. and Du, D.-M. *Org. Lett.* **2018**, 20, 3797.

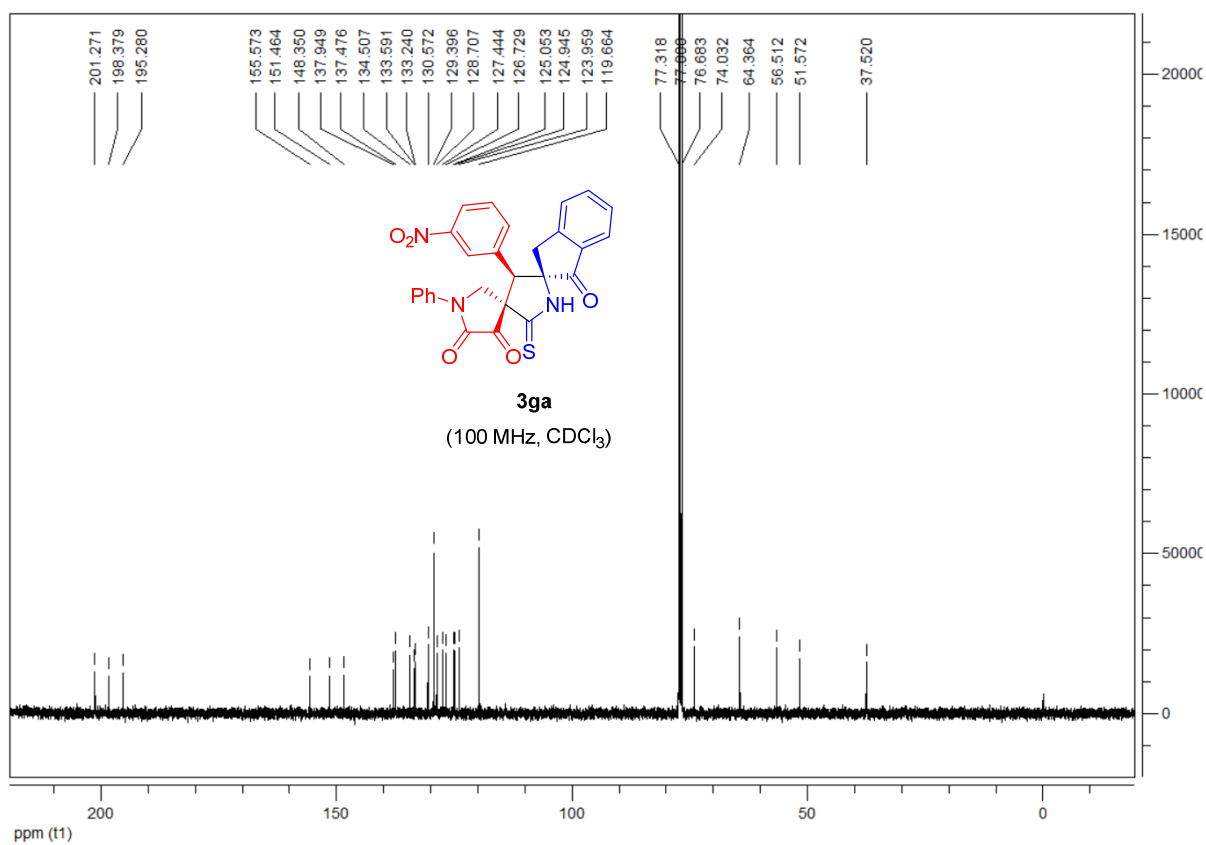
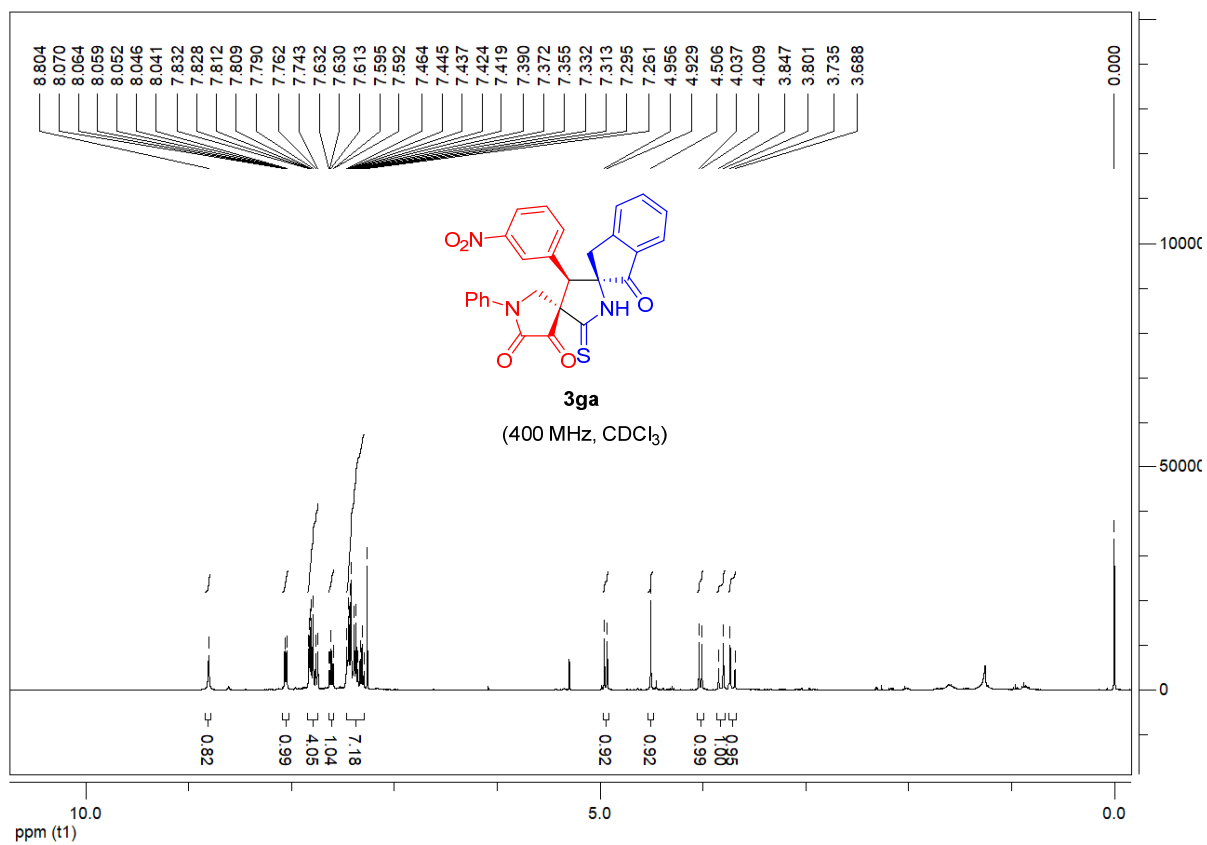
7. Copies of ^1H and ^{13}C NMR spectra of new products

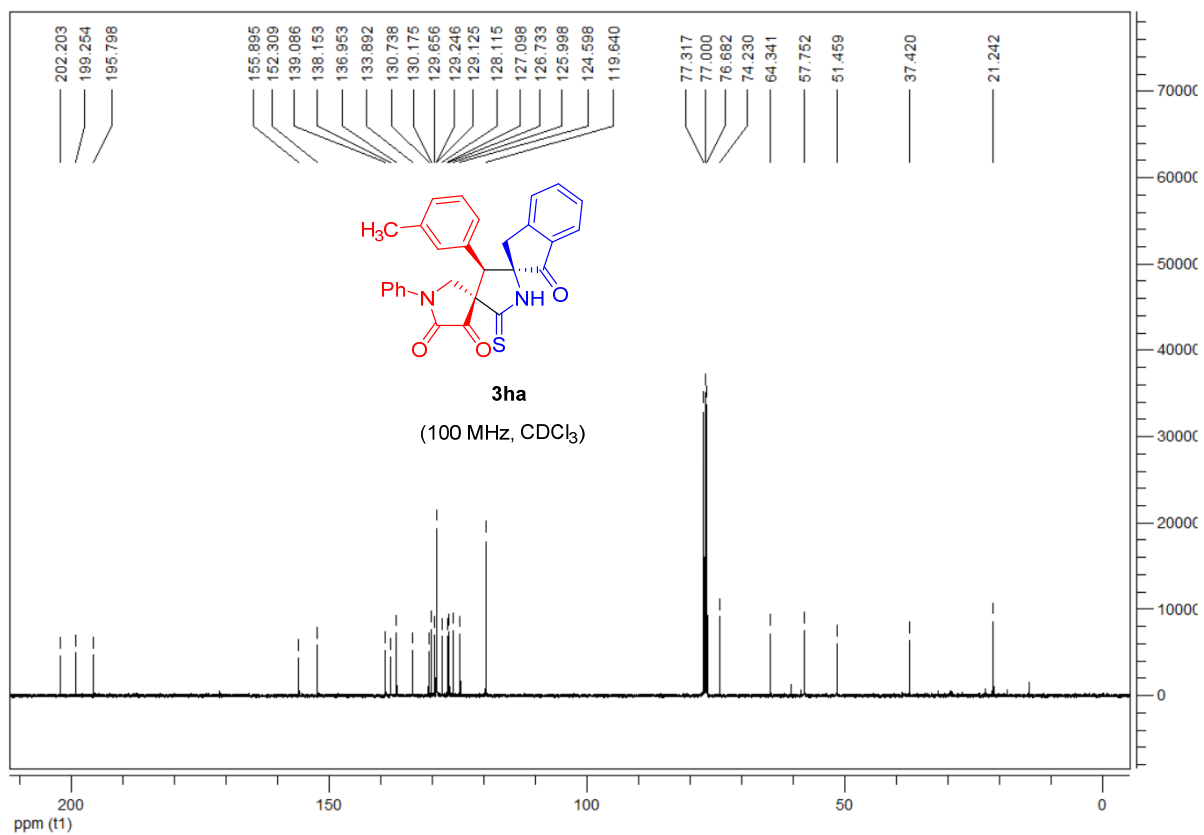
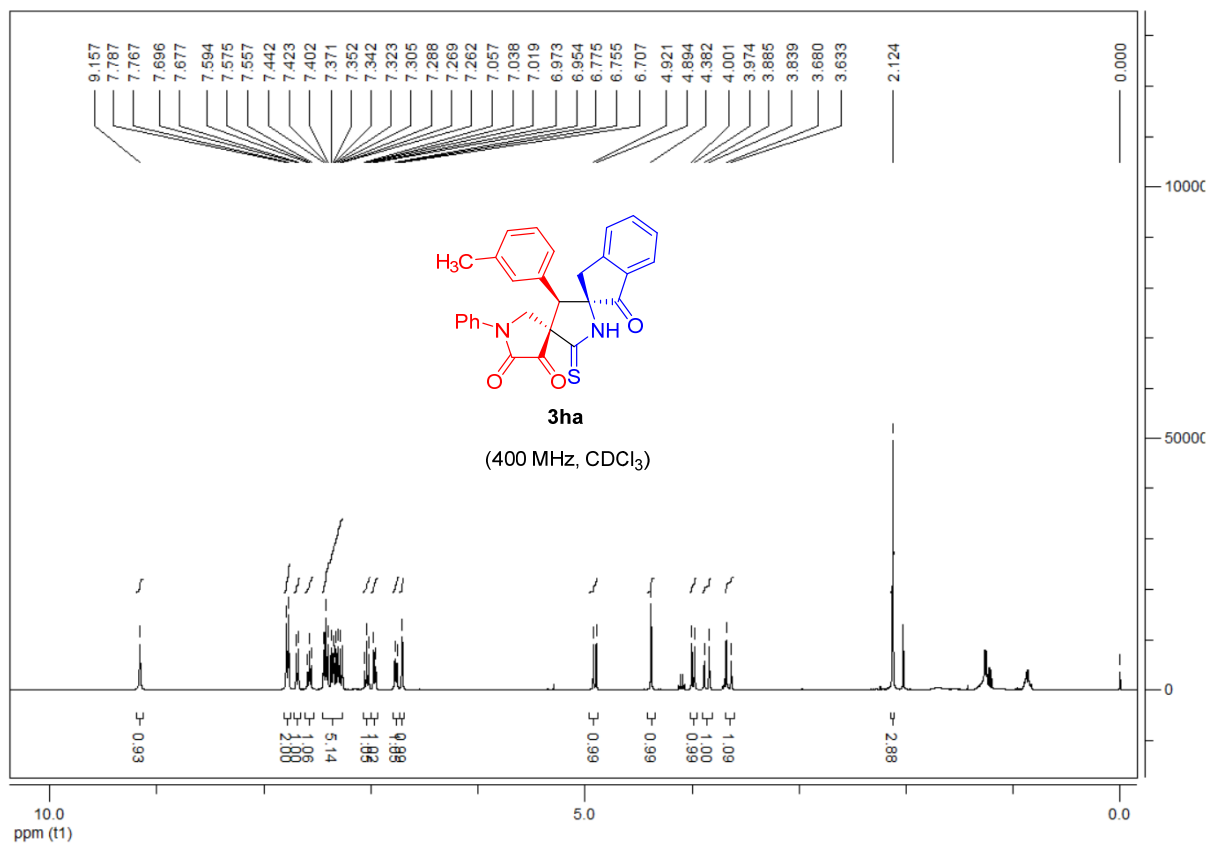


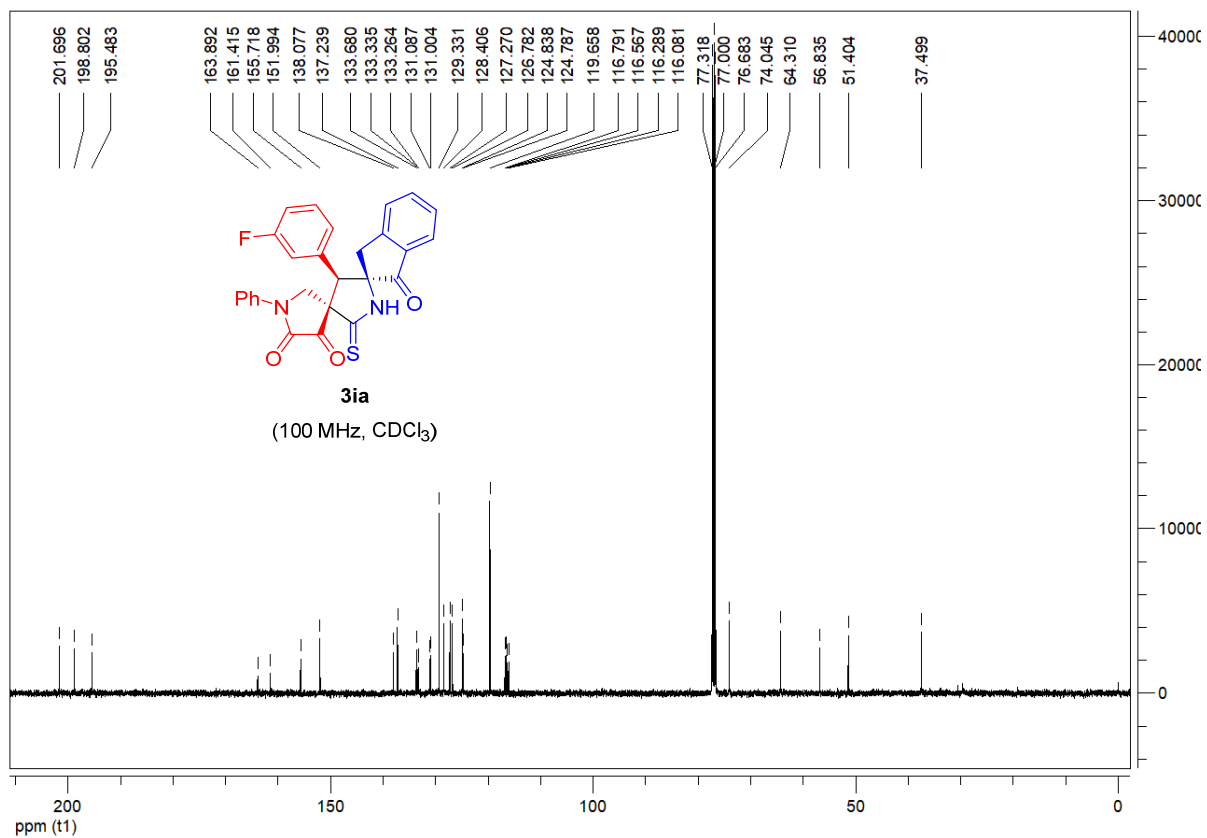
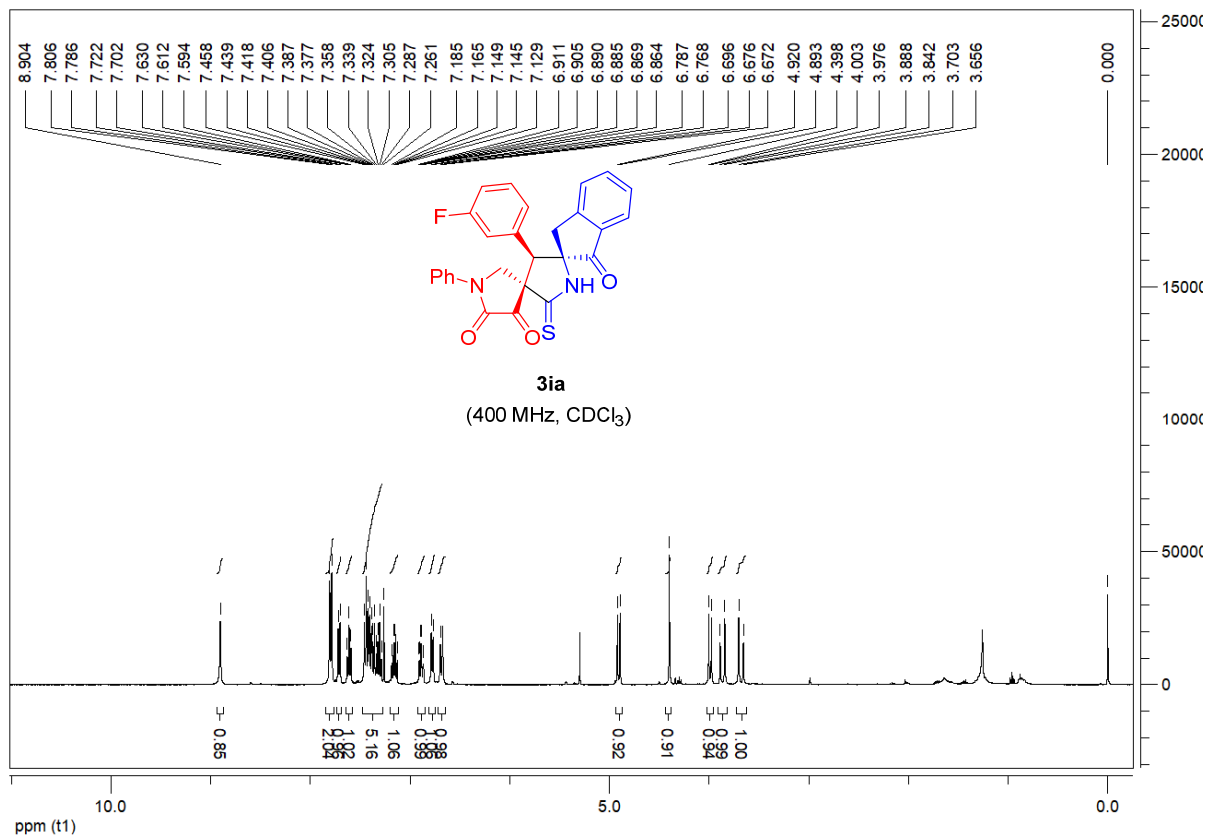


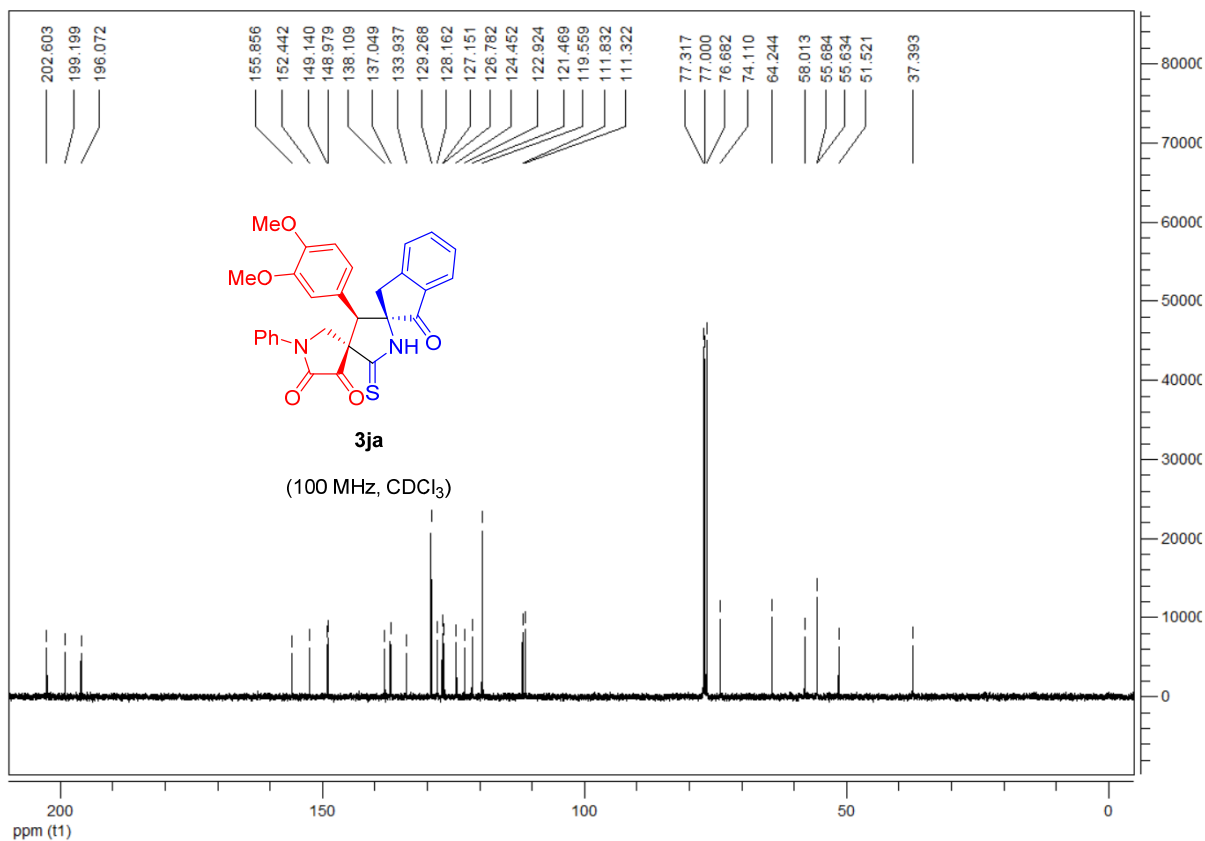
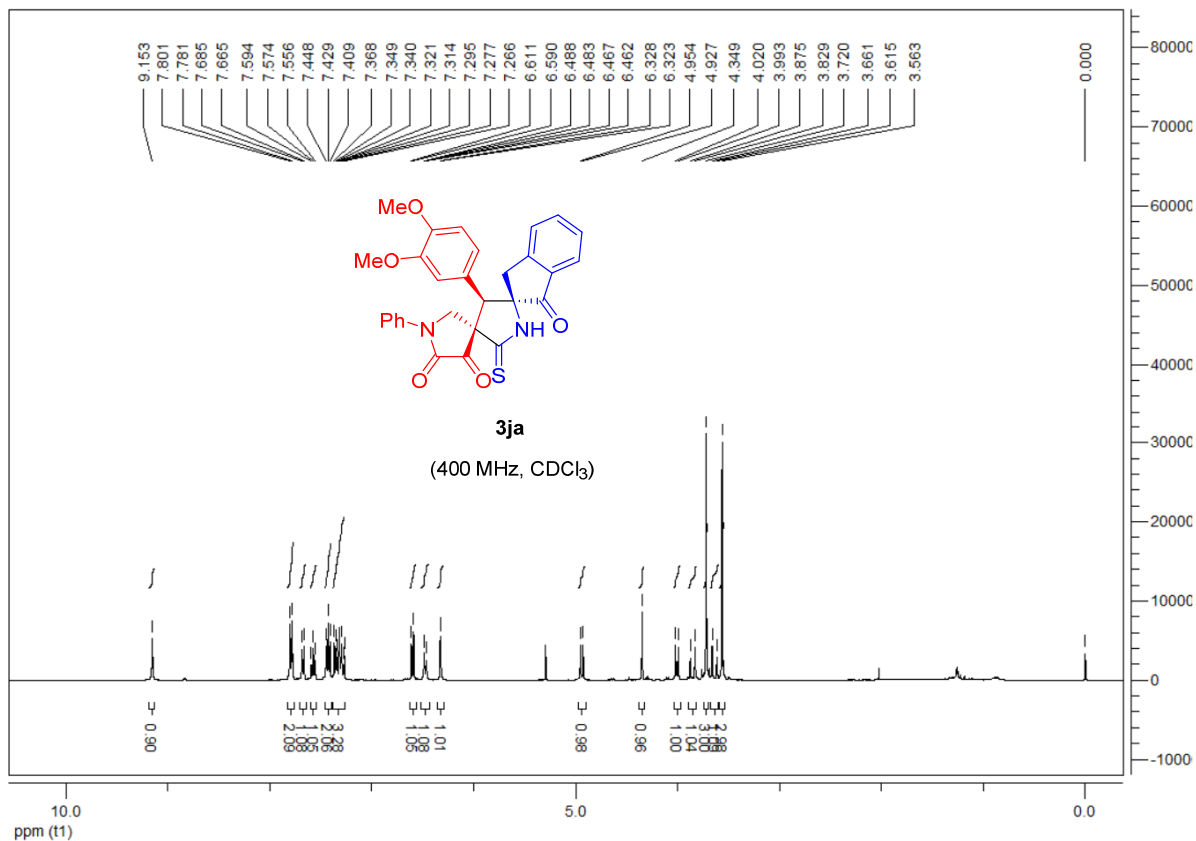


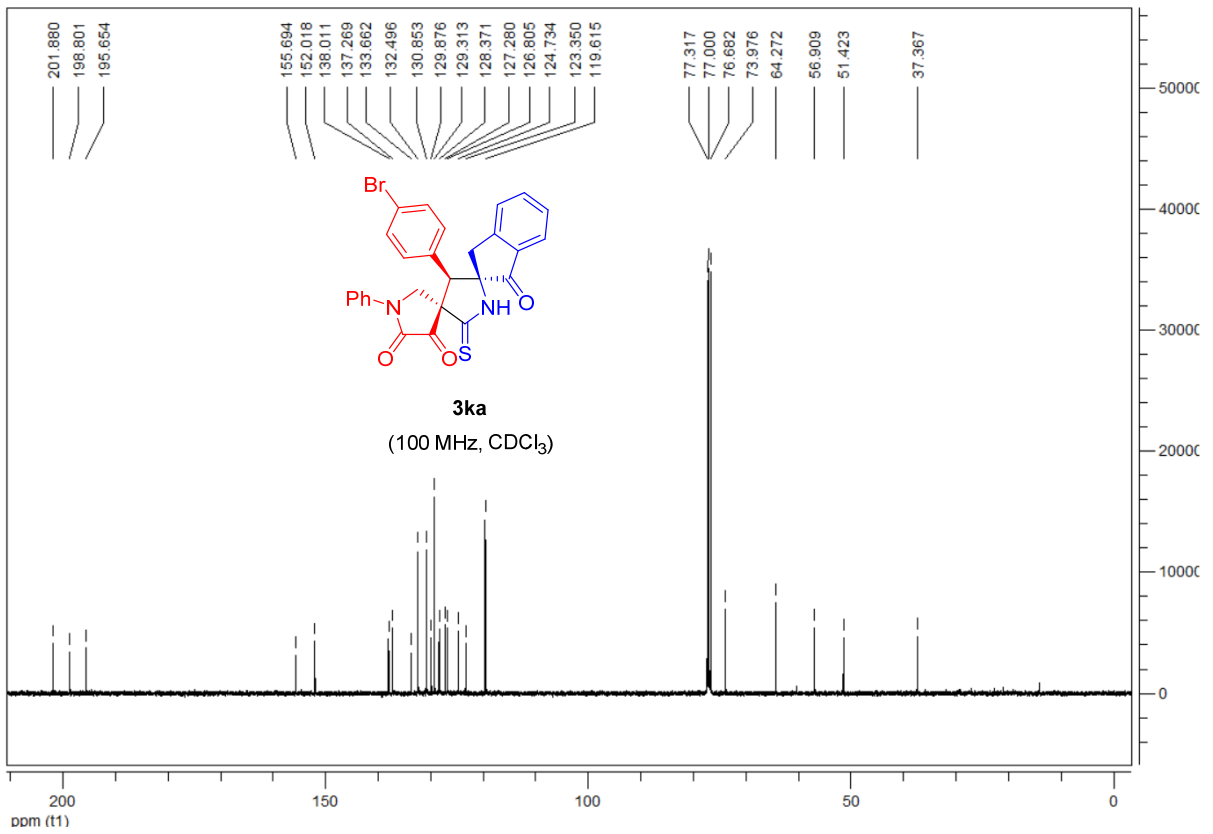
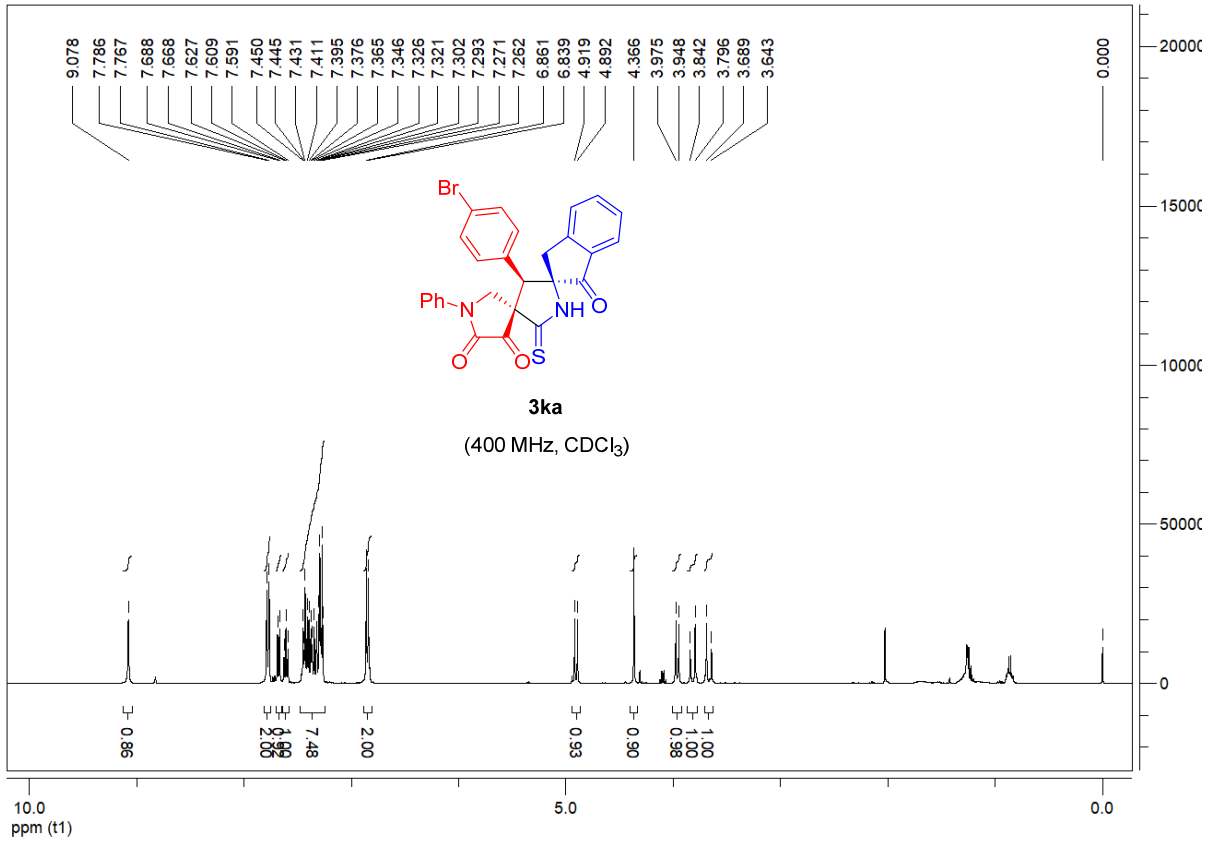


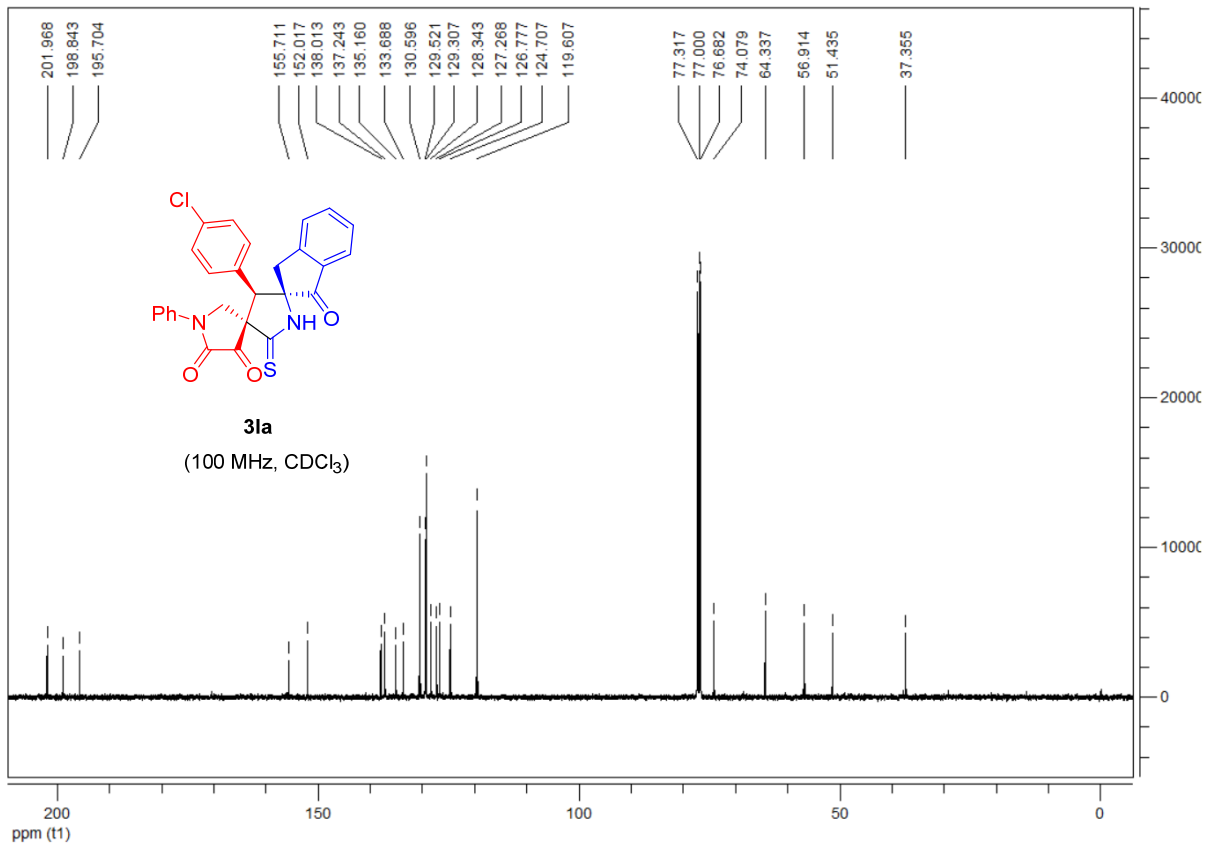
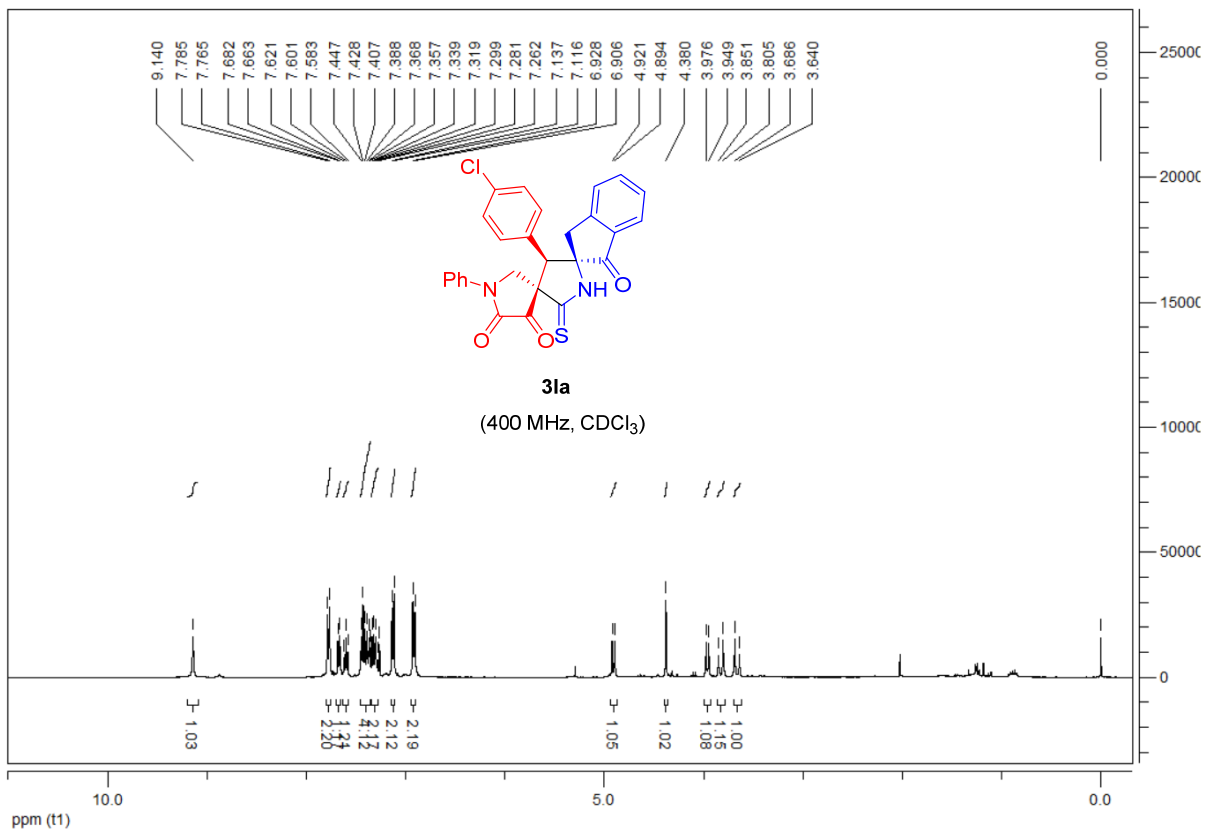


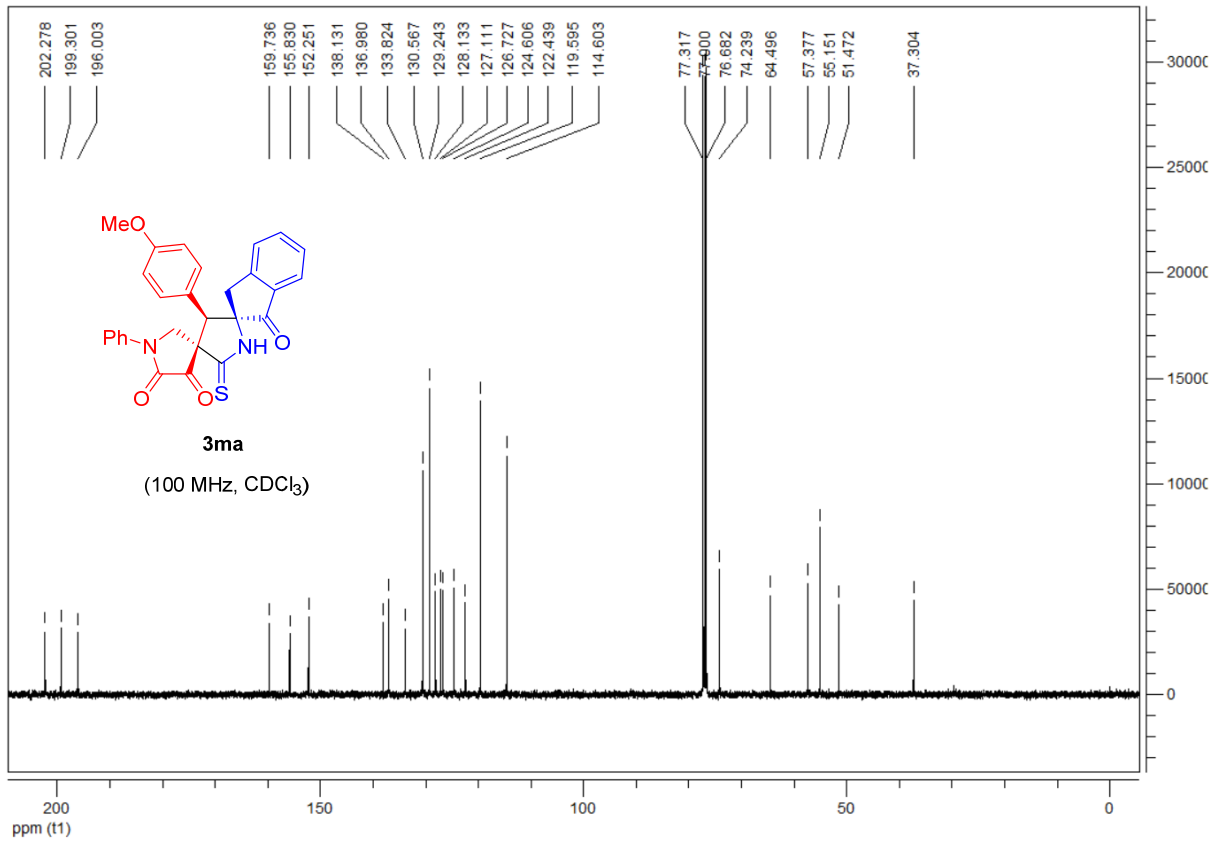
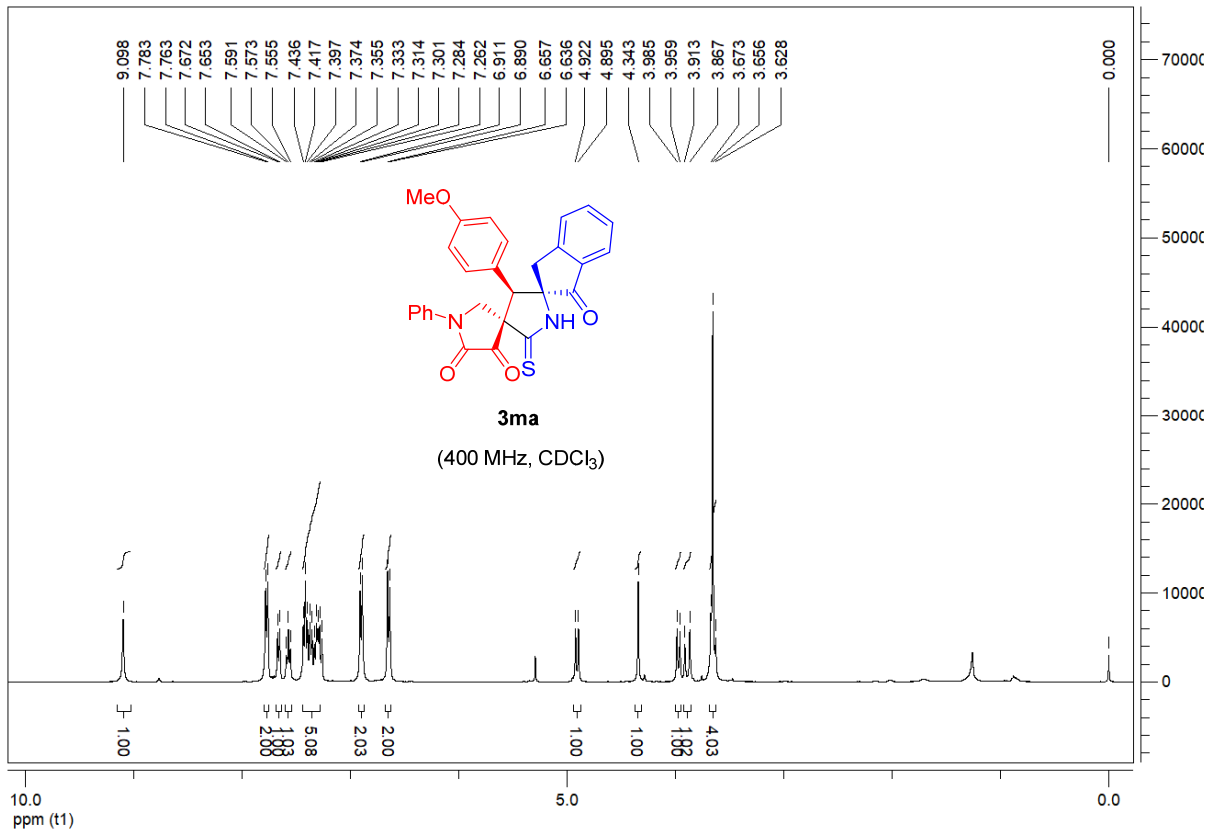


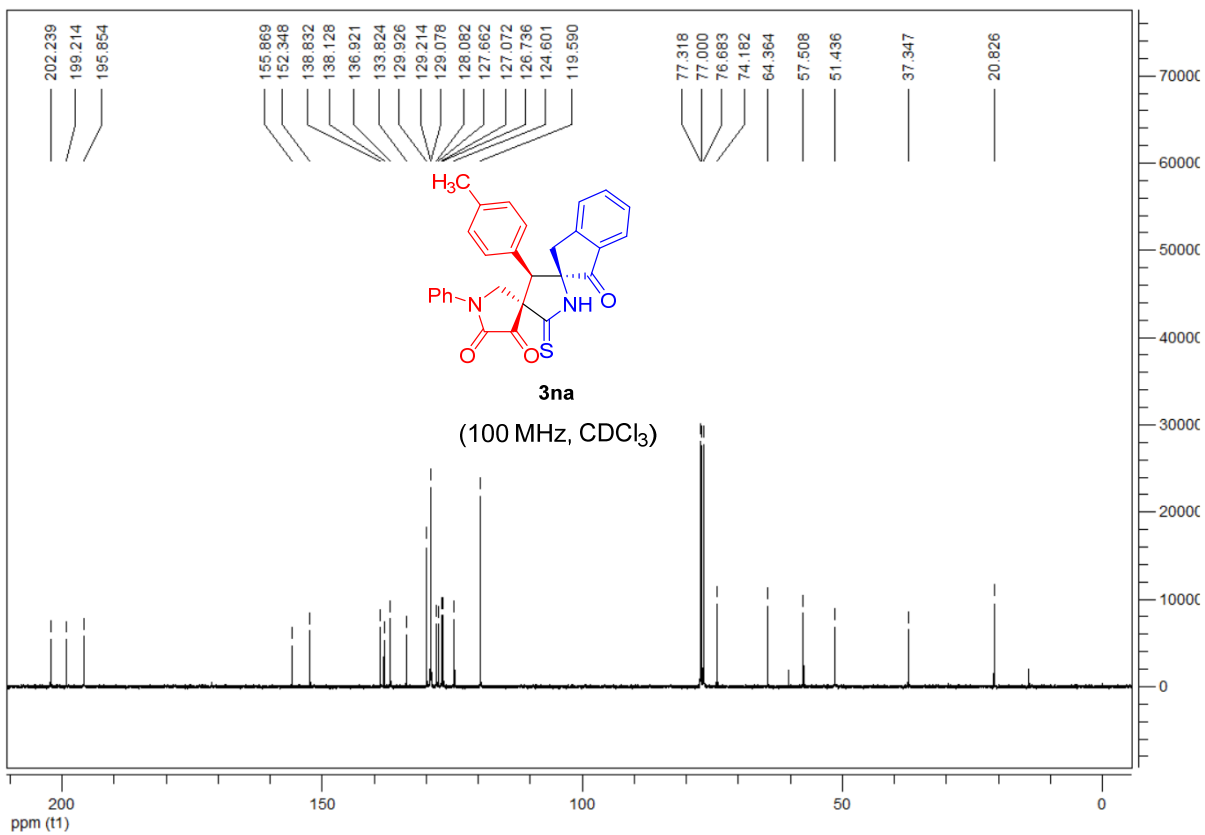
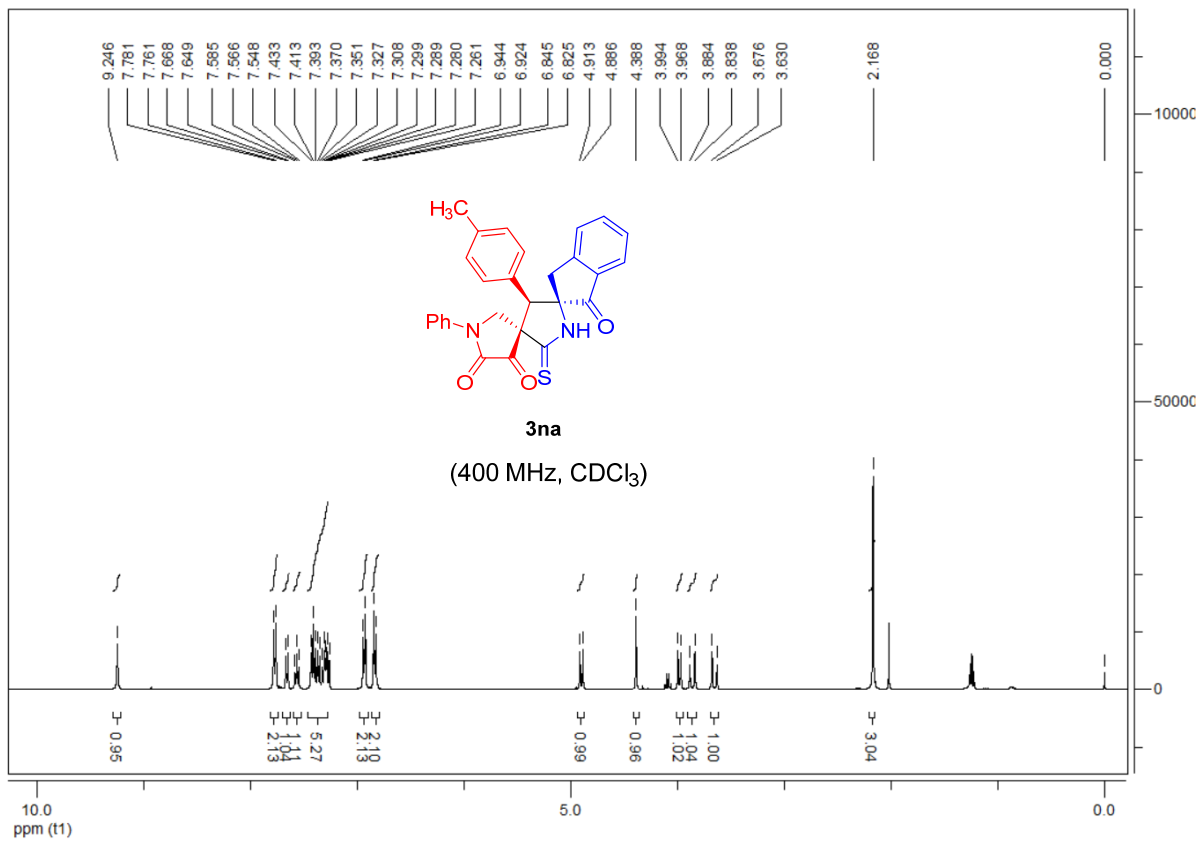


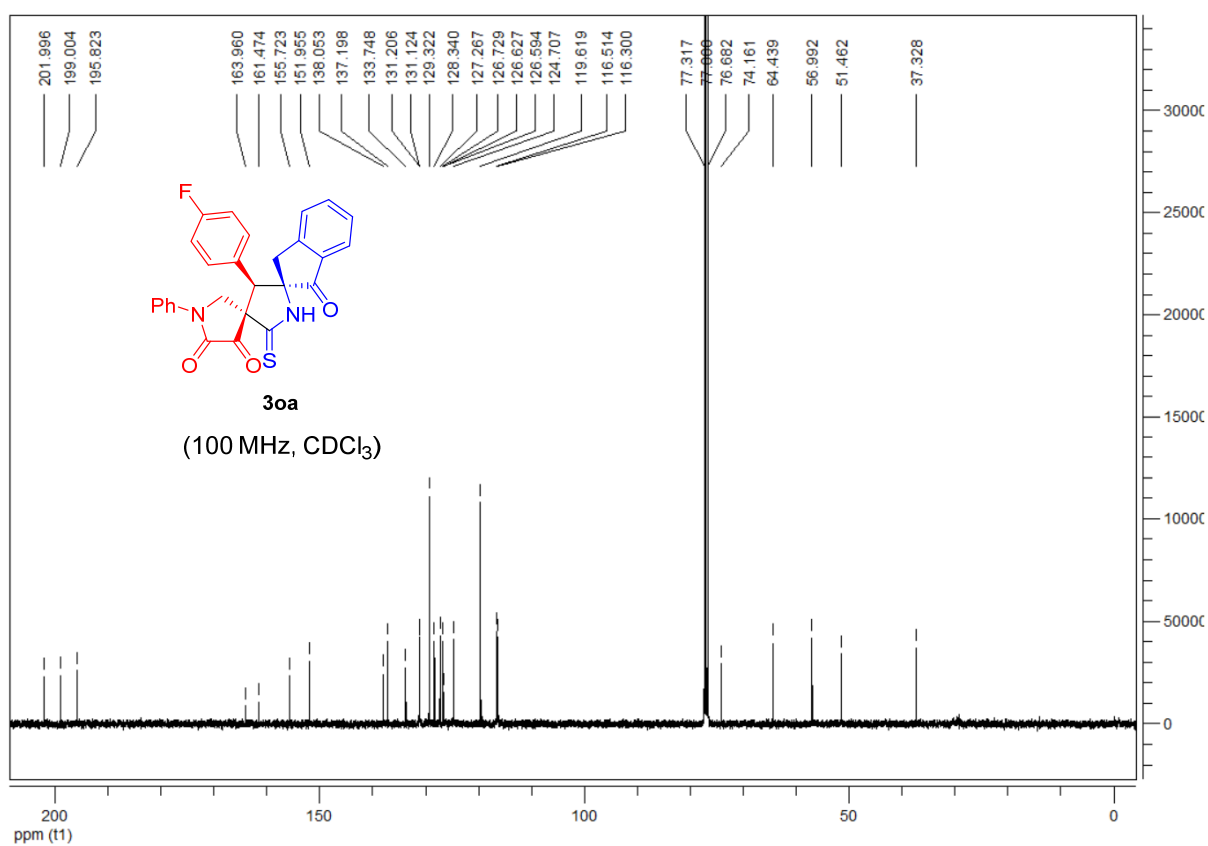
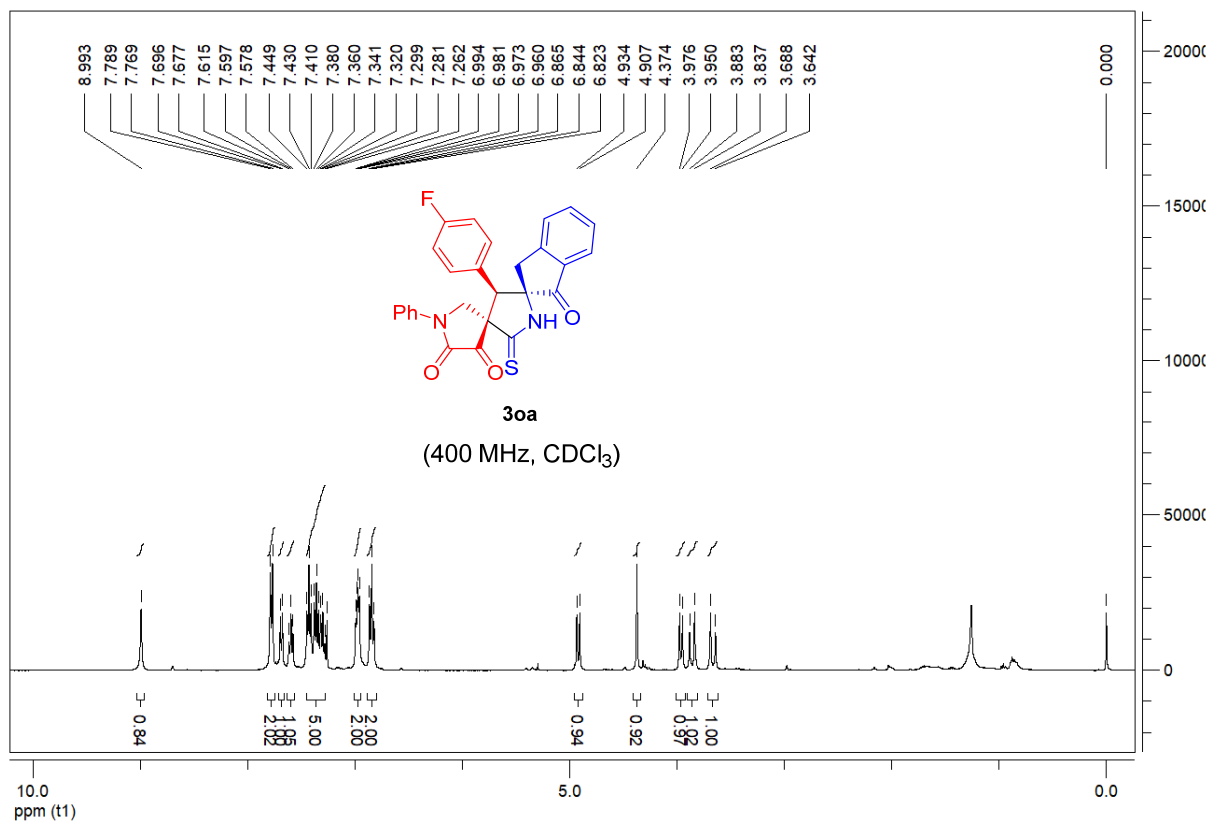


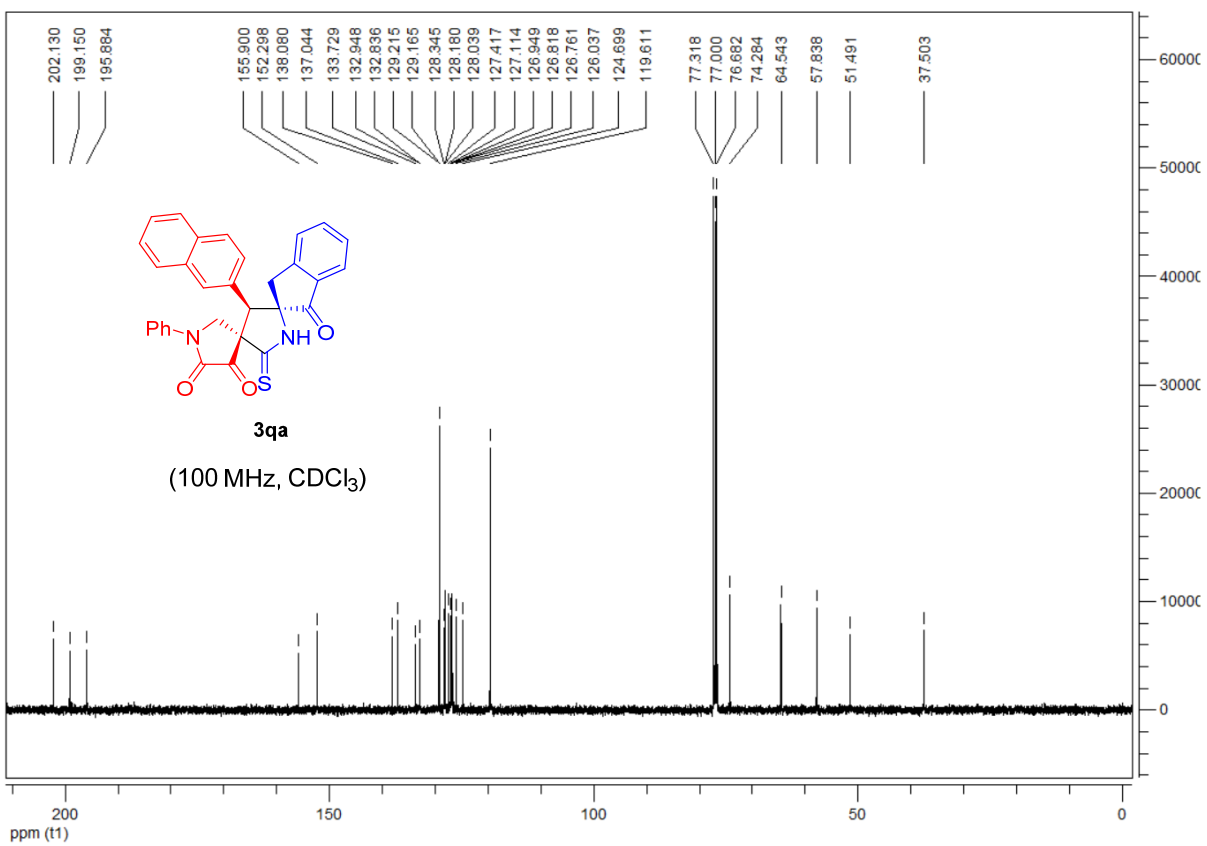
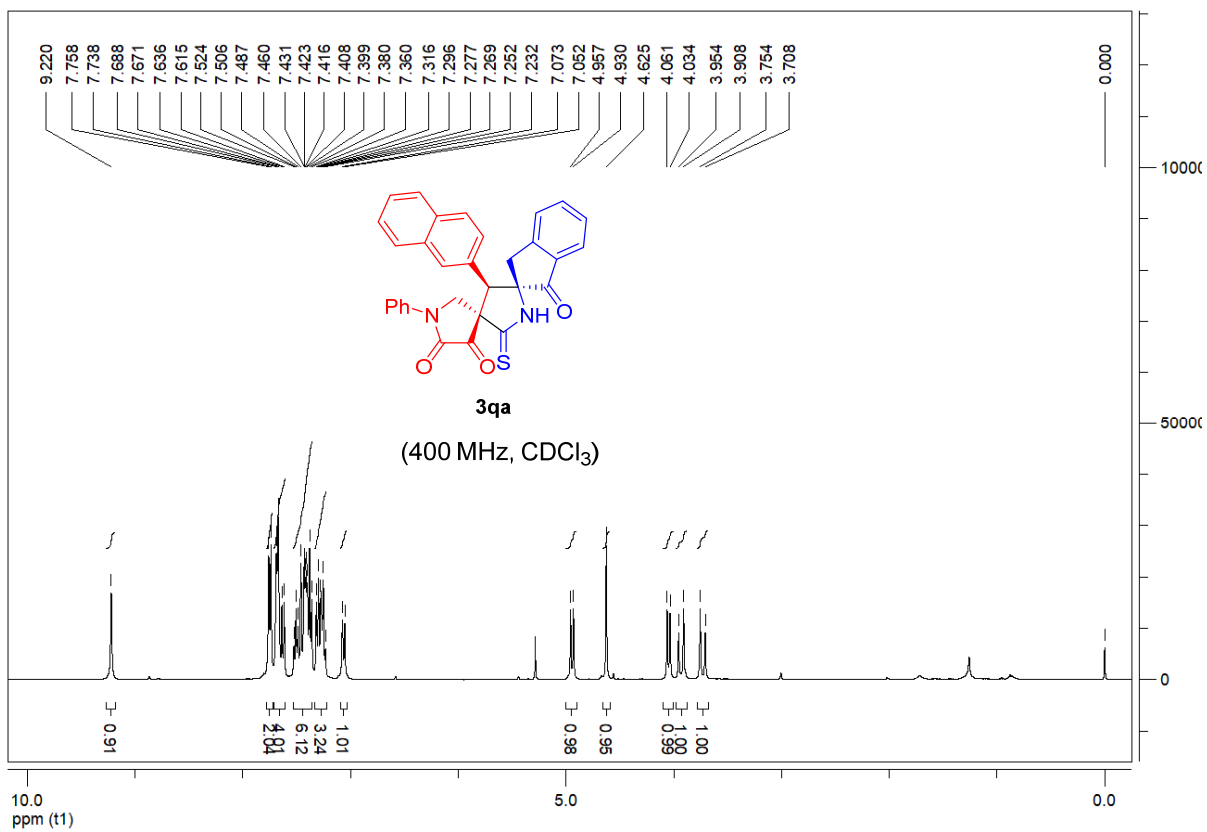


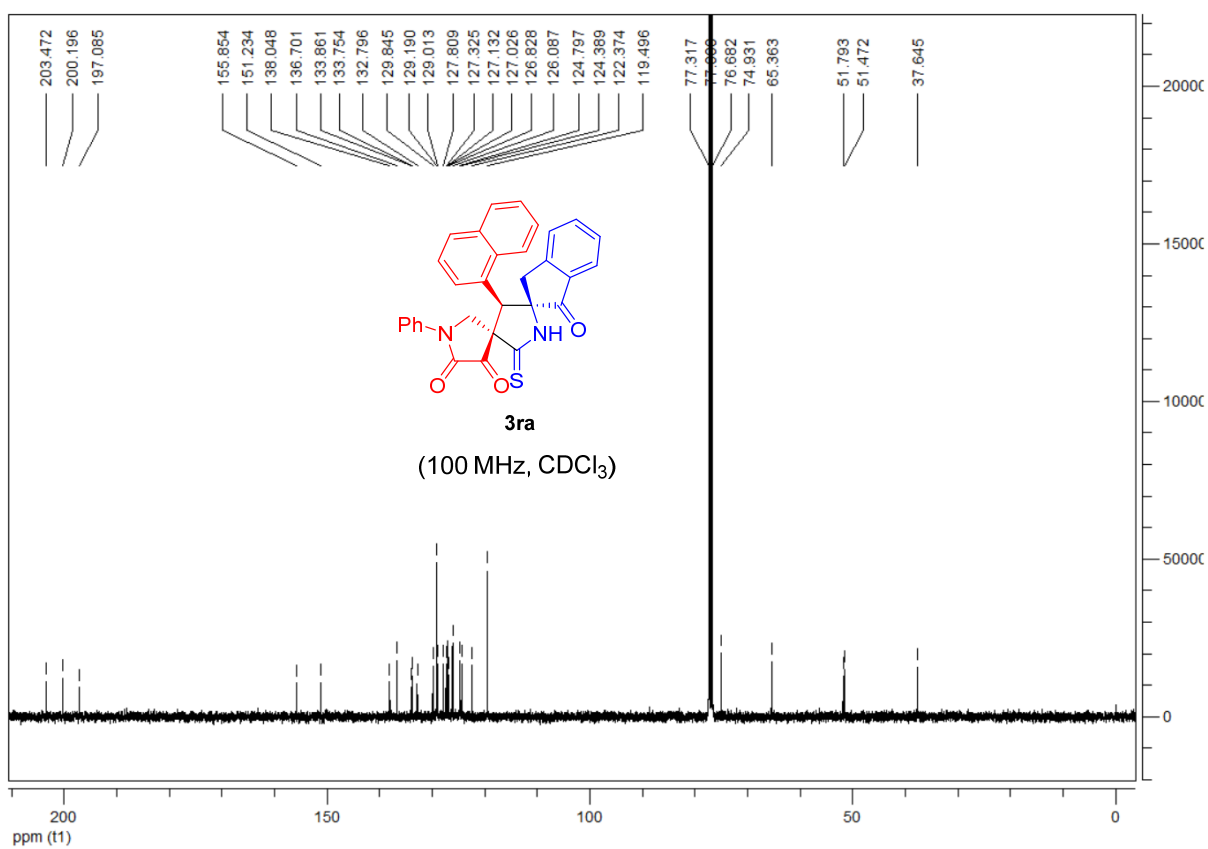
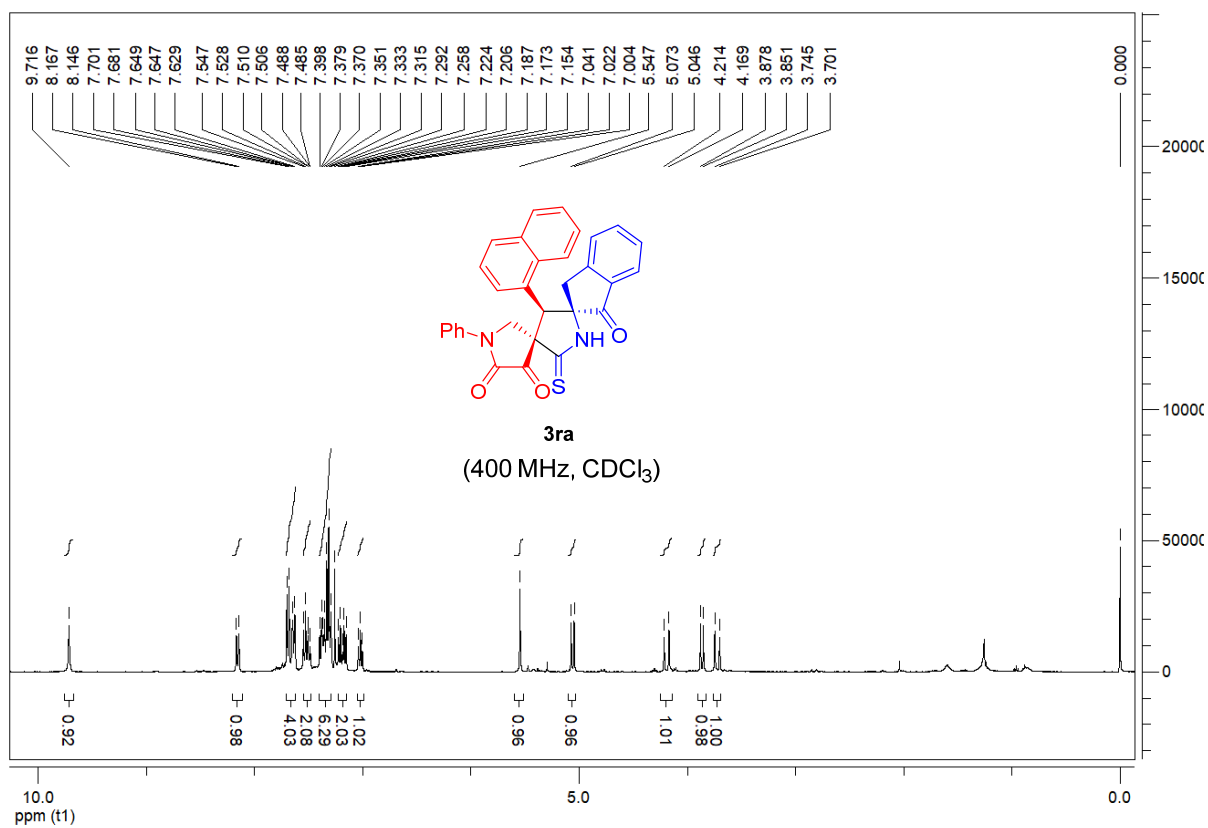


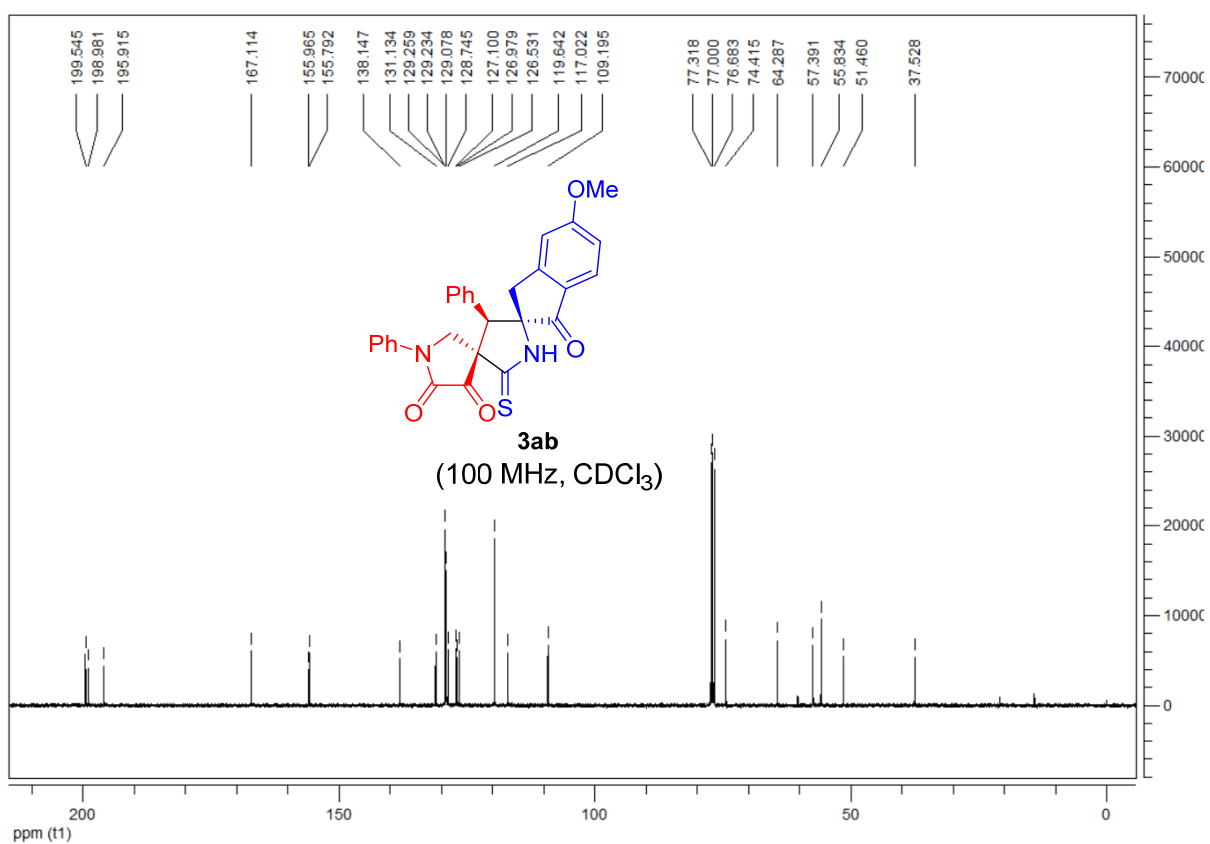
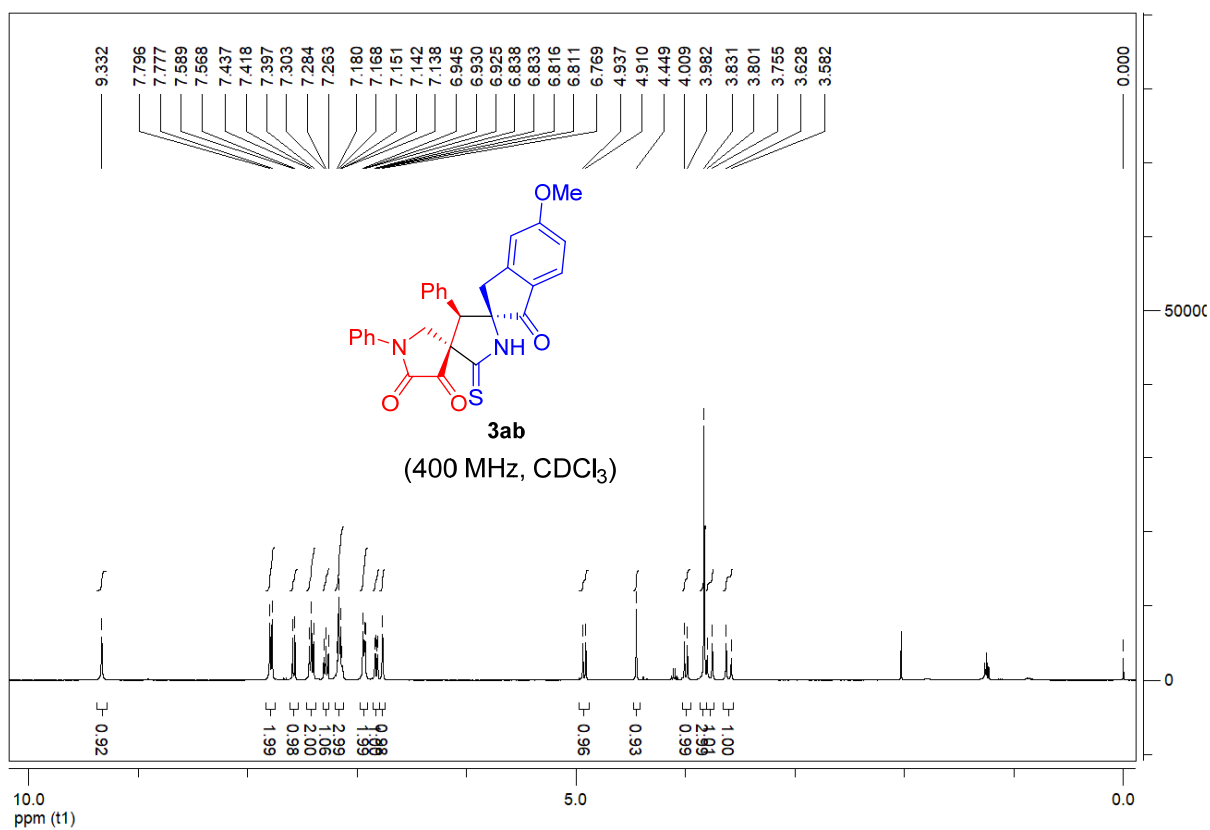


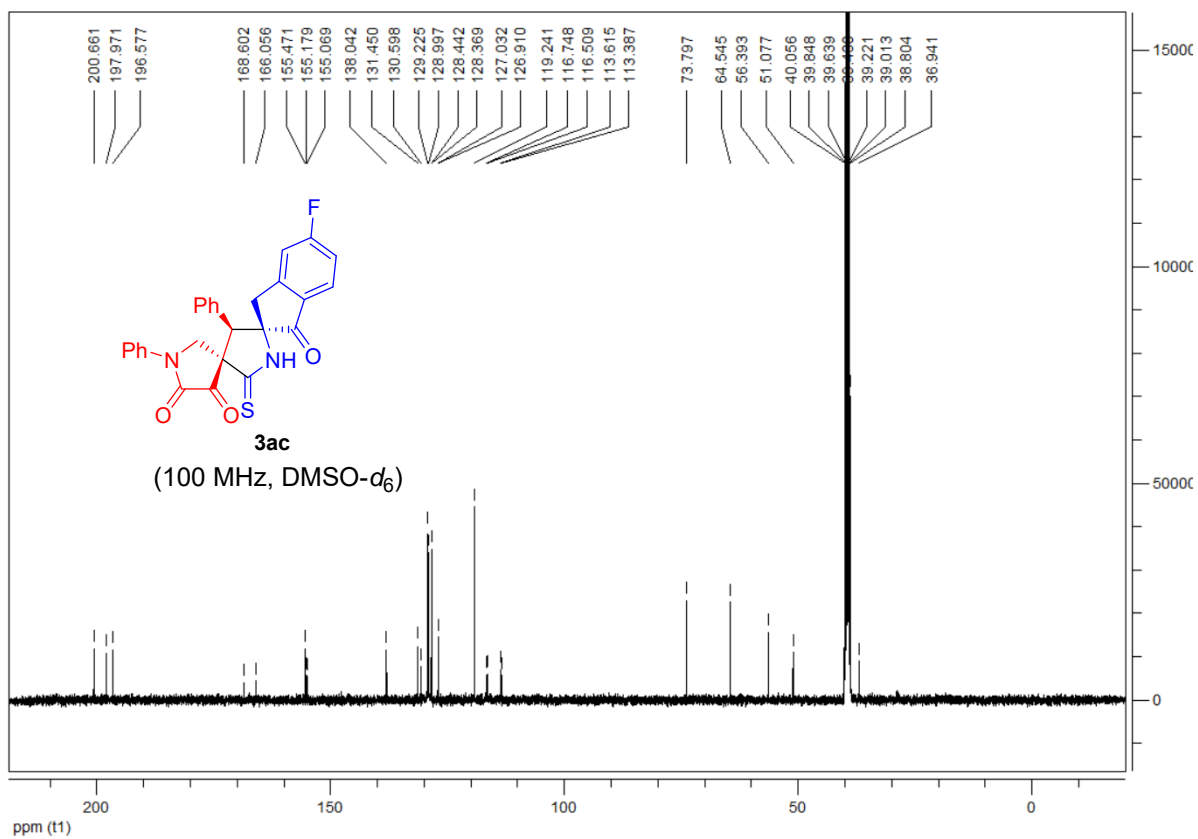
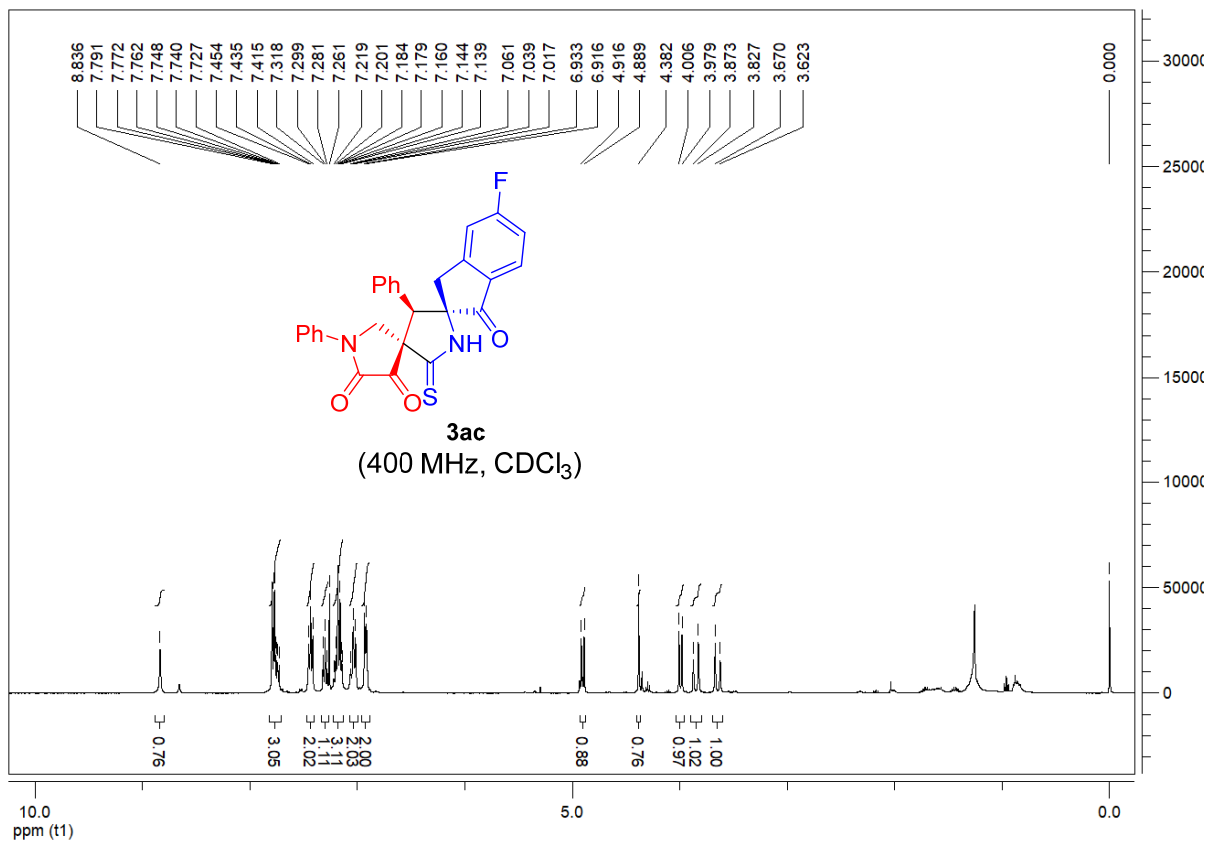


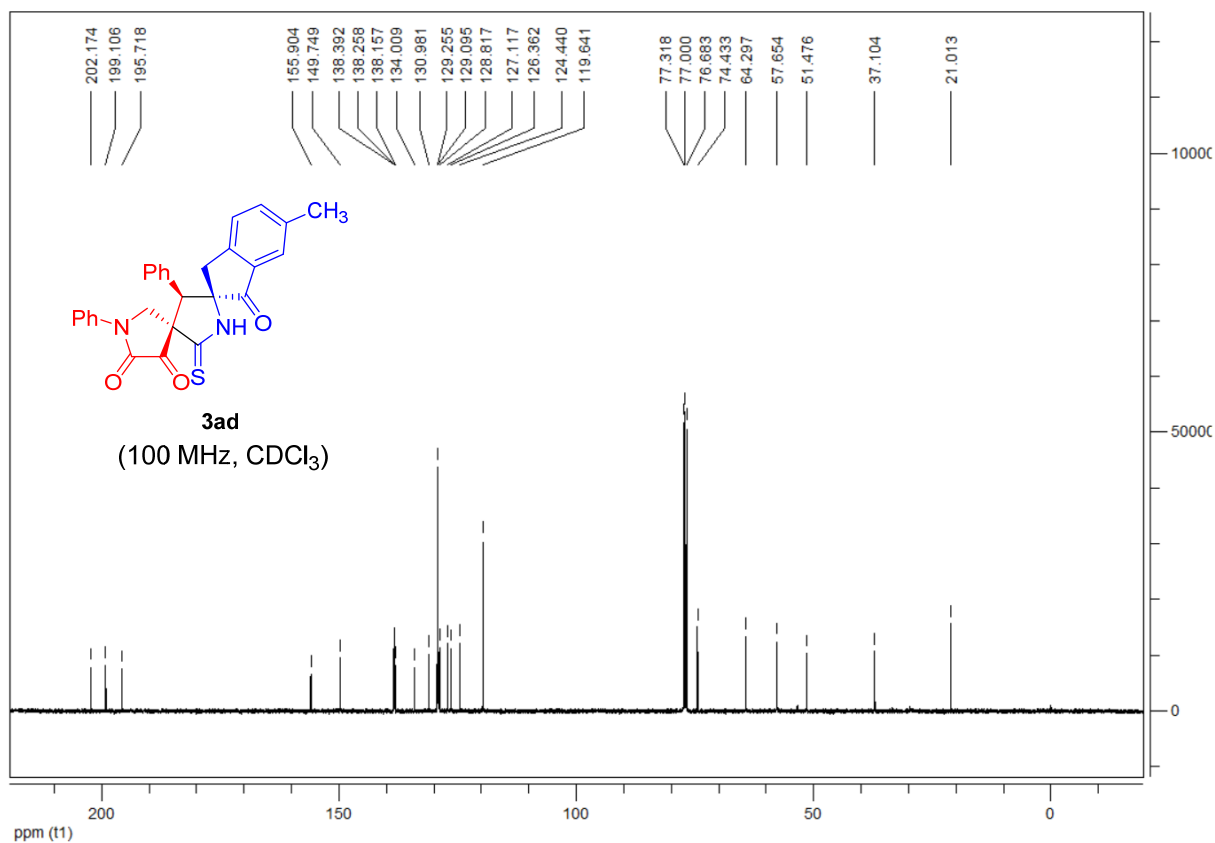
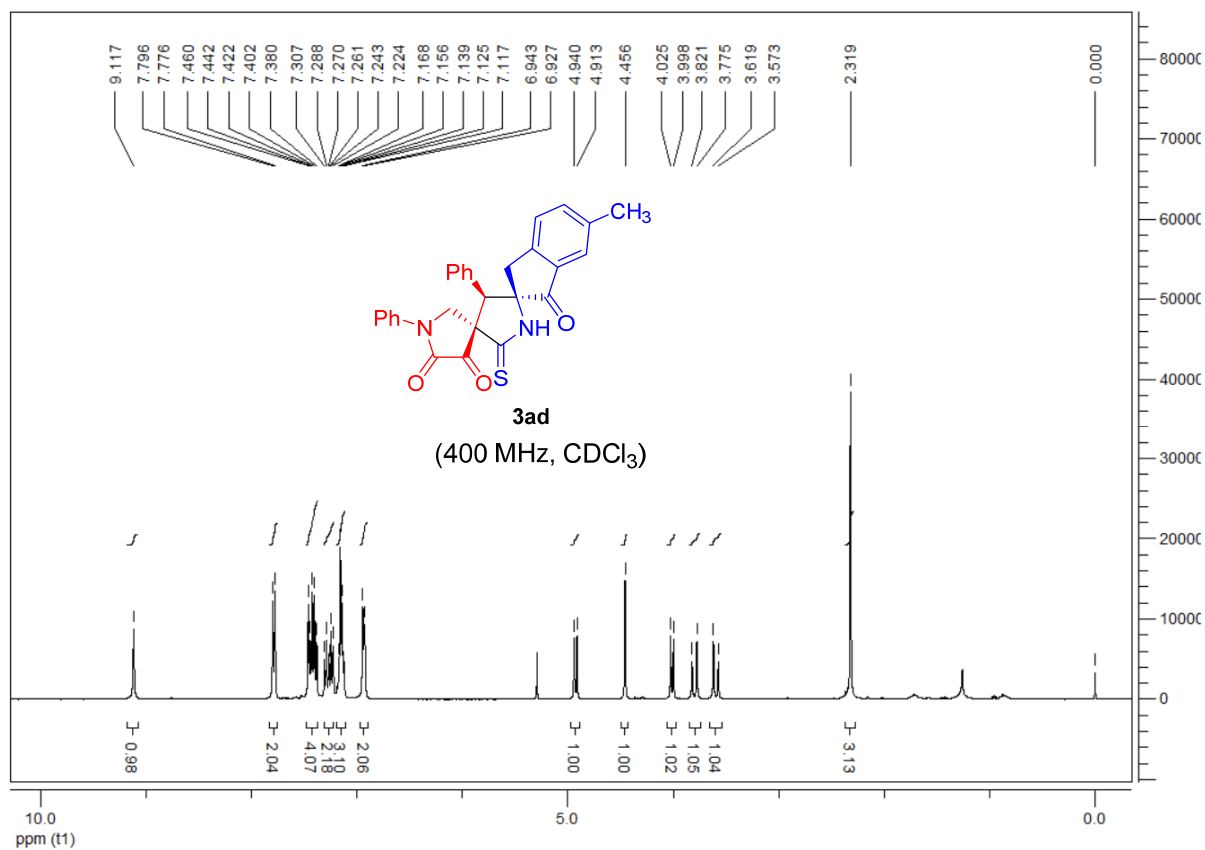


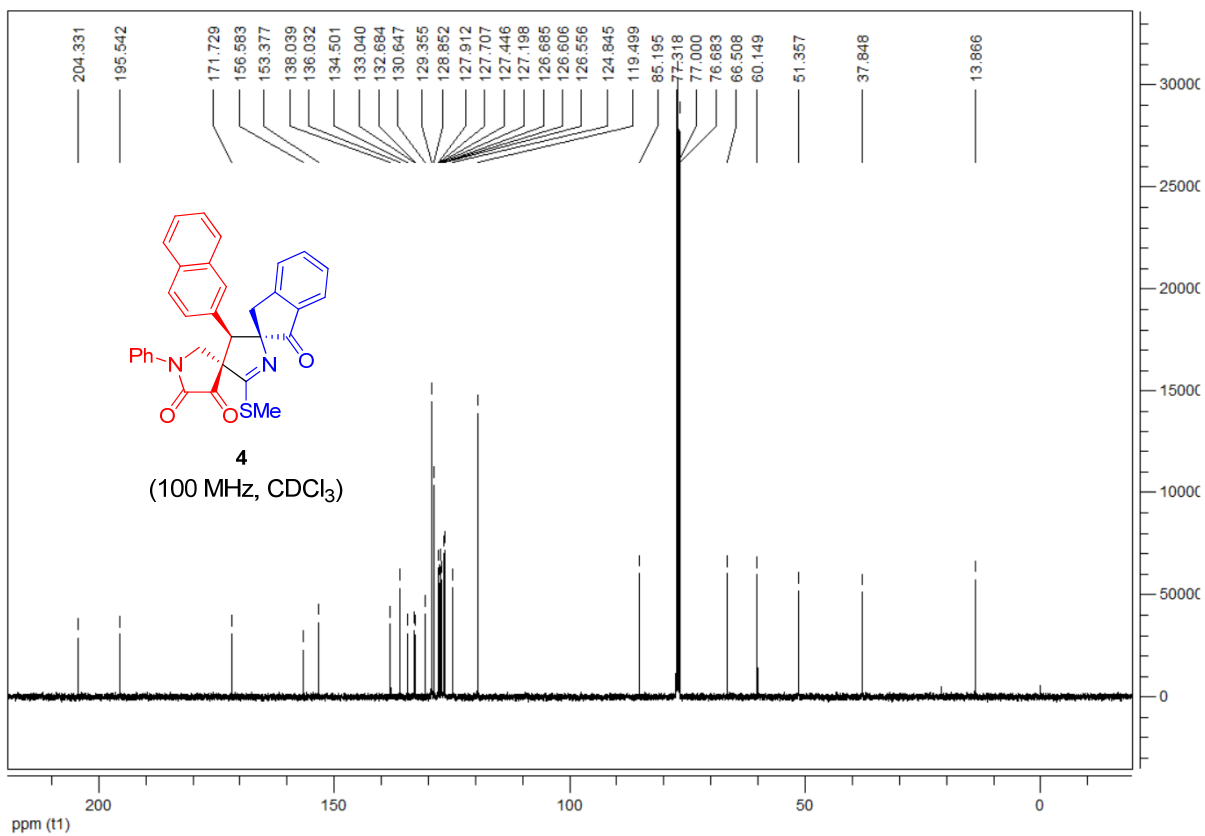
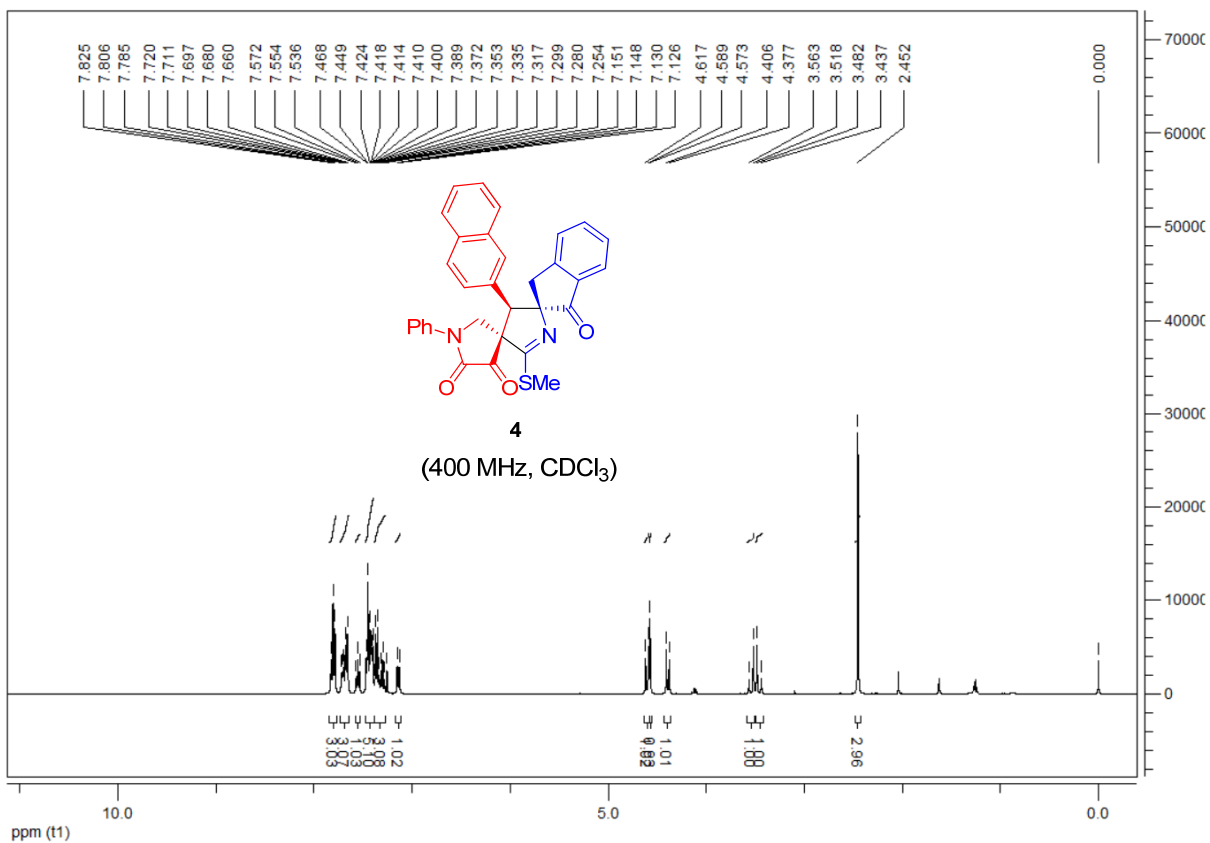




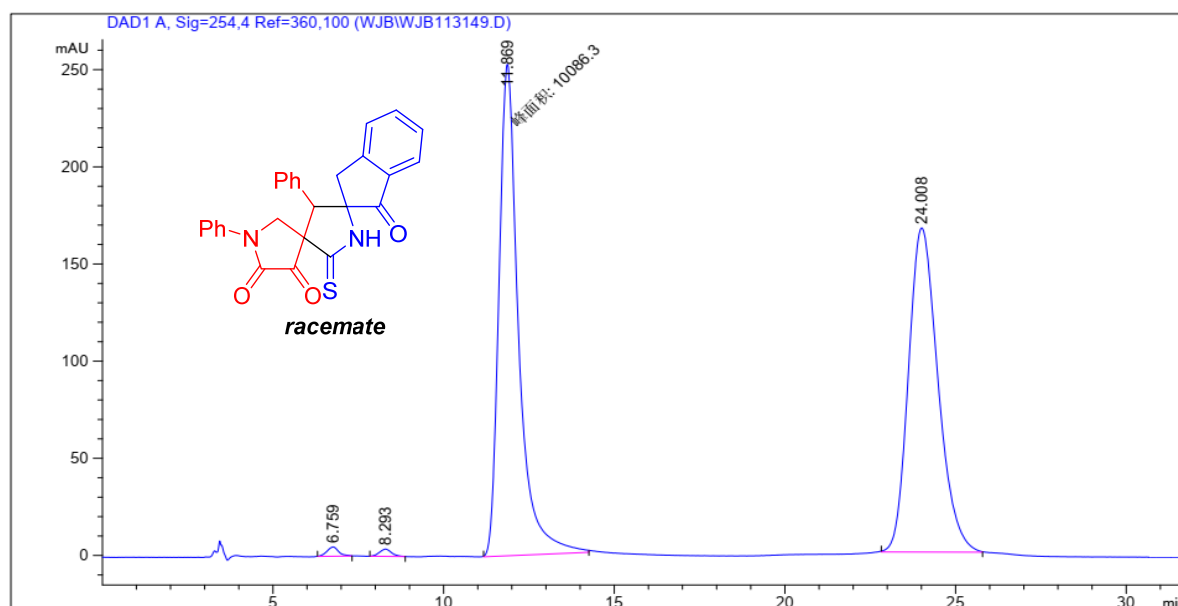




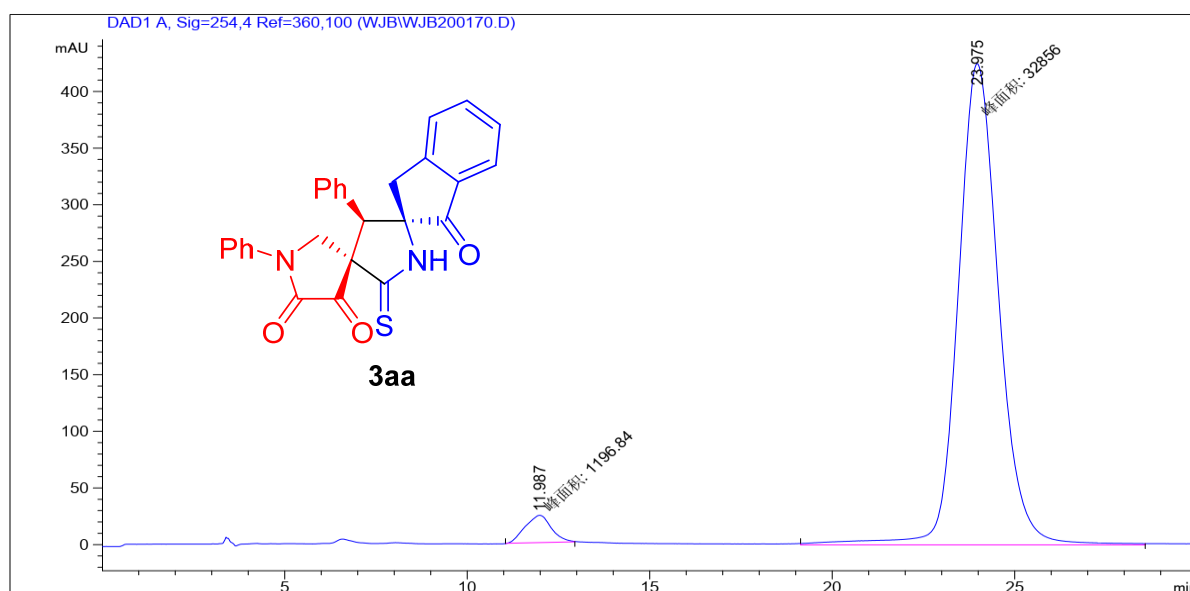




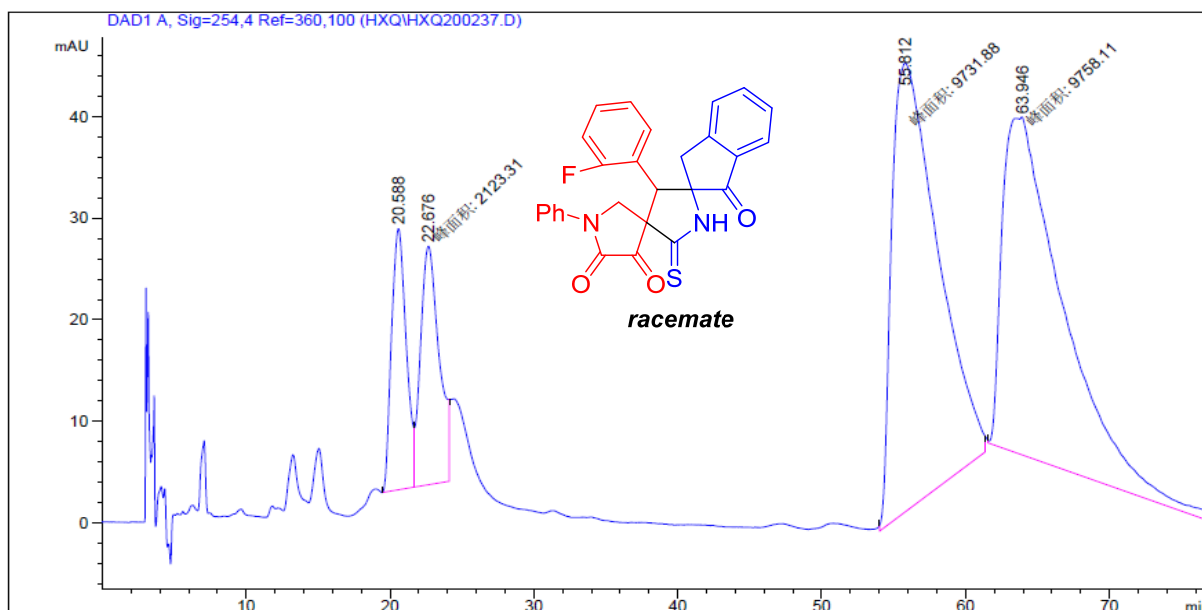
8. Copies of HPLC chromatograms of new products



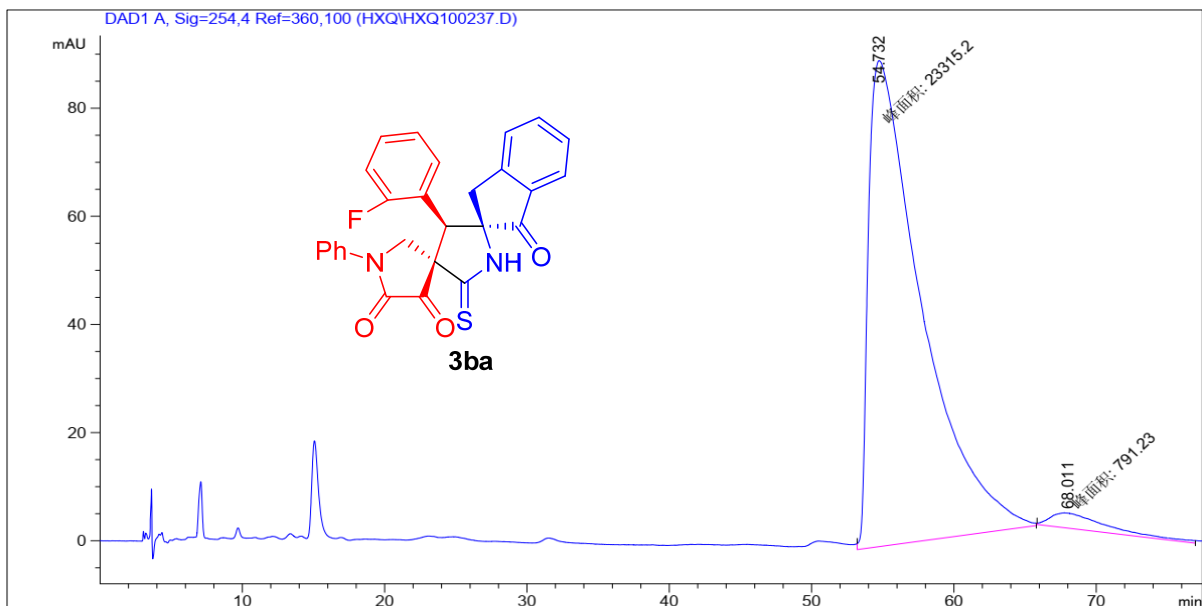
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2	8.293	BB	0.3223	92.31229	3.76140	0.4547
3	11.869	MM	0.6647	1.00863e4	252.91548	49.6797
4	24.008	BB	0.8962	1.00104e4	166.79616	49.3060



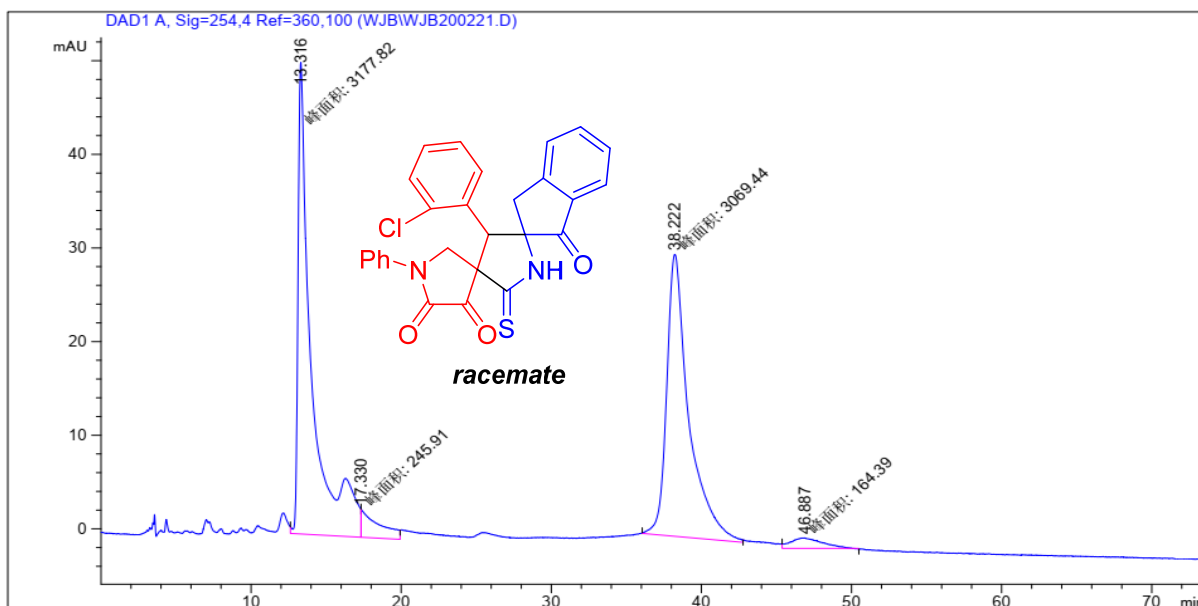
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2	23.975	MM	1.2892	3.28560e4	424.76688	96.4853



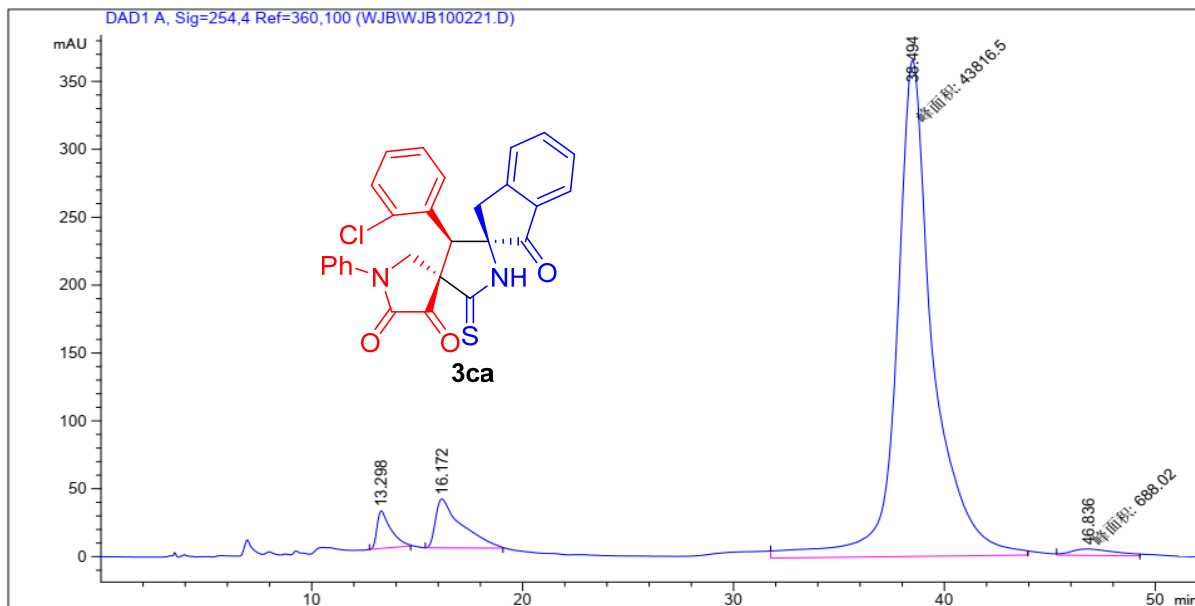
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2	22.676	MF	1.5067	2123.31372	23.48732	9.0608
3	55.812	MM	2.5848	9731.87598	44.18242	41.5288
4	63.946	MM	4.8931	9758.10840	33.23734	41.6408



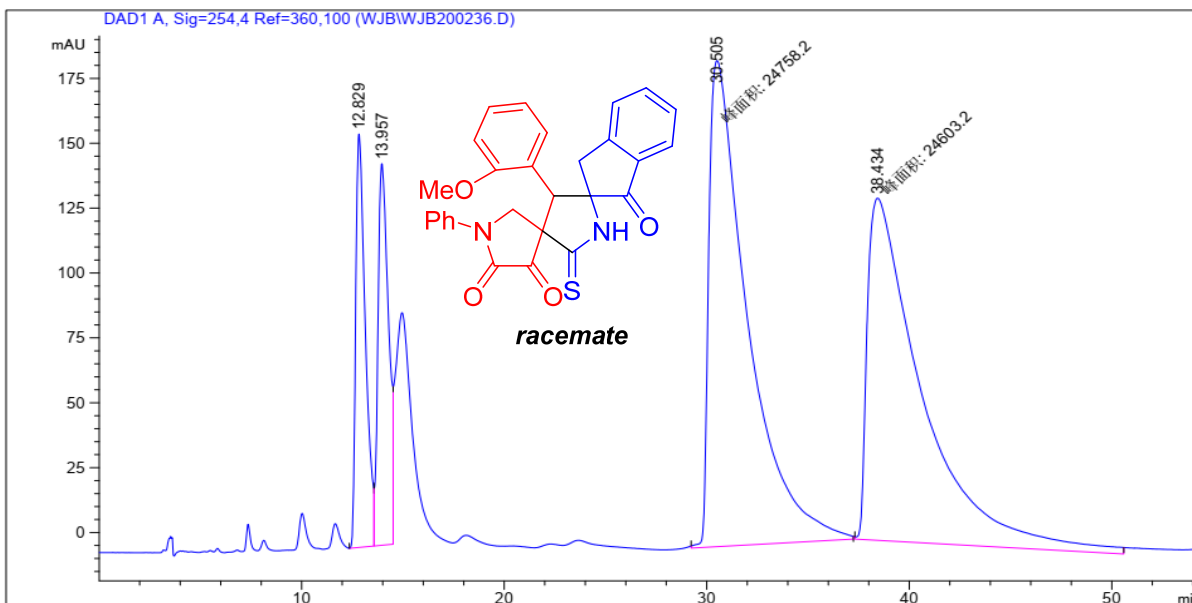
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	54.732	MM	4.3238	2.33152e4	89.87164	96.7178
2	68.011	MM	4.7572	791.23035	2.77205	3.2822



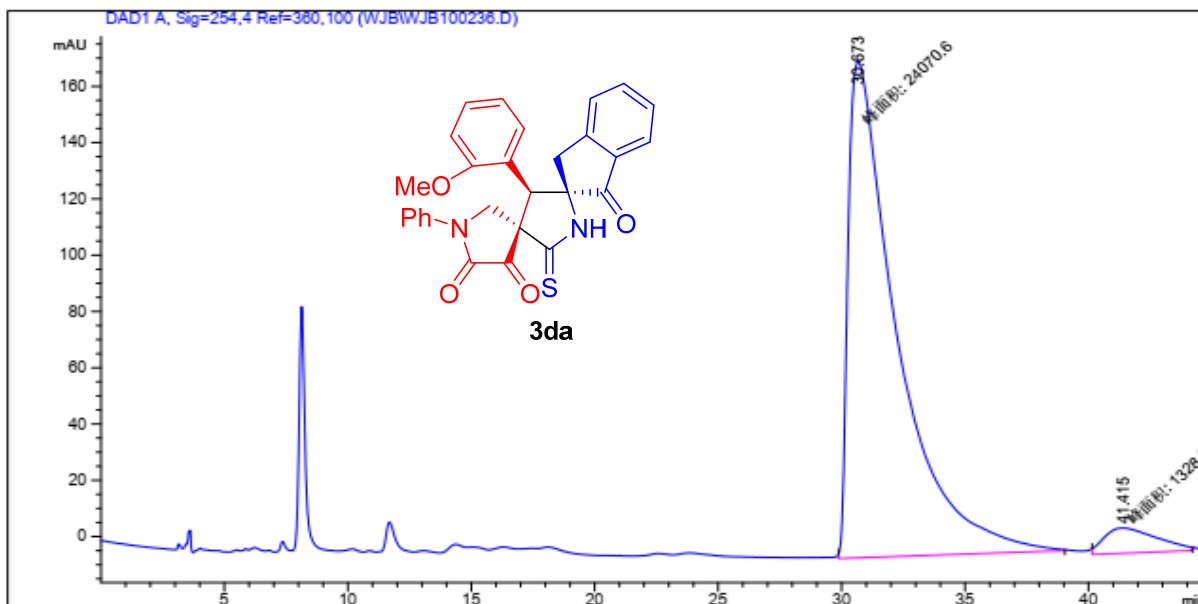
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.316	MF	1.0517	3177.82007	50.36149	47.7325
2	17.330	FM	1.3670	245.91020	2.99811	3.6937
3	38.222	MM	1.6997	3069.43701	30.09769	46.1046
4	46.887	MM	2.4579	164.39032	1.11470	2.4692



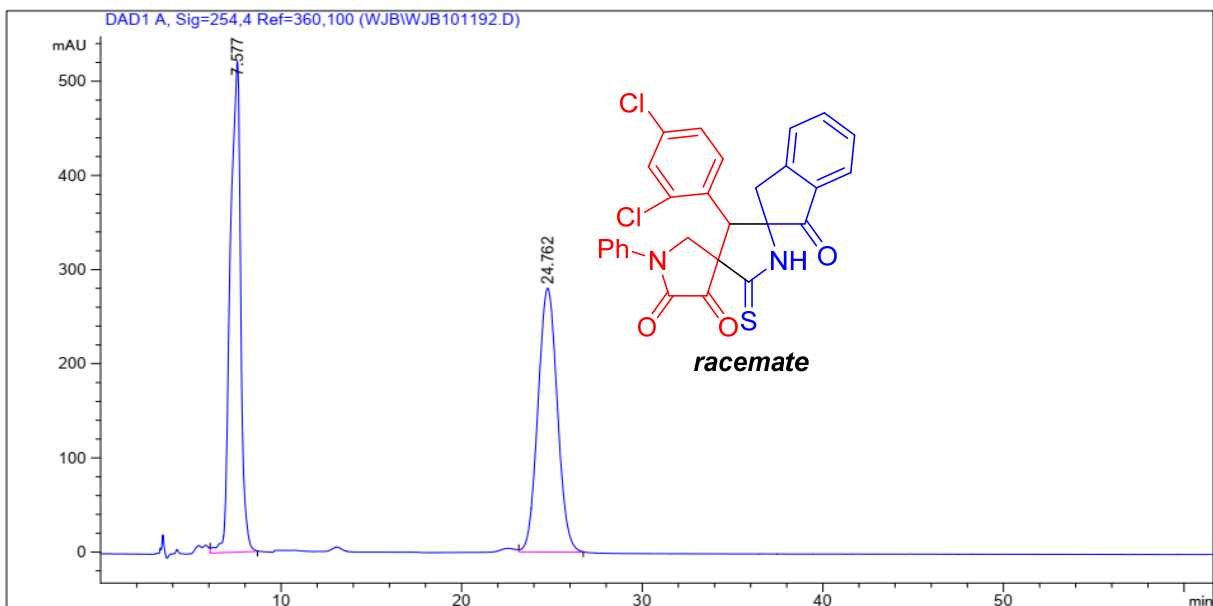
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.298	BB	0.6299	1256.66870	27.66854	2.5730
2	16.172	BB	1.1270	3079.28052	36.03431	6.3048
3	38.494	MM	1.9972	4.38165e4	365.65387	89.7135
4	46.836	MM	2.4574	688.01984	4.66636	1.4087



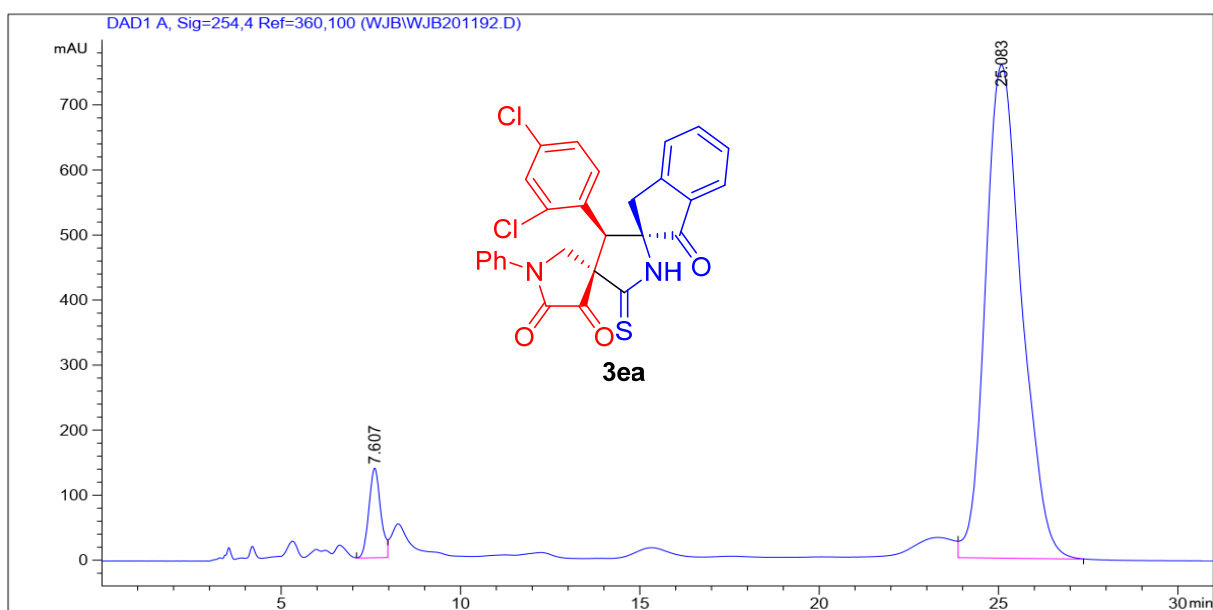
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.829	BV	0.4956	5293.69092	159.33244	8.8291
2	13.957	VV	0.5487	5302.12256	147.04448	8.8432
3	30.505	MM	2.2032	2.47582e4	187.28592	41.2931
4	38.434	MM	3.1091	2.46032e4	131.88596	41.0346



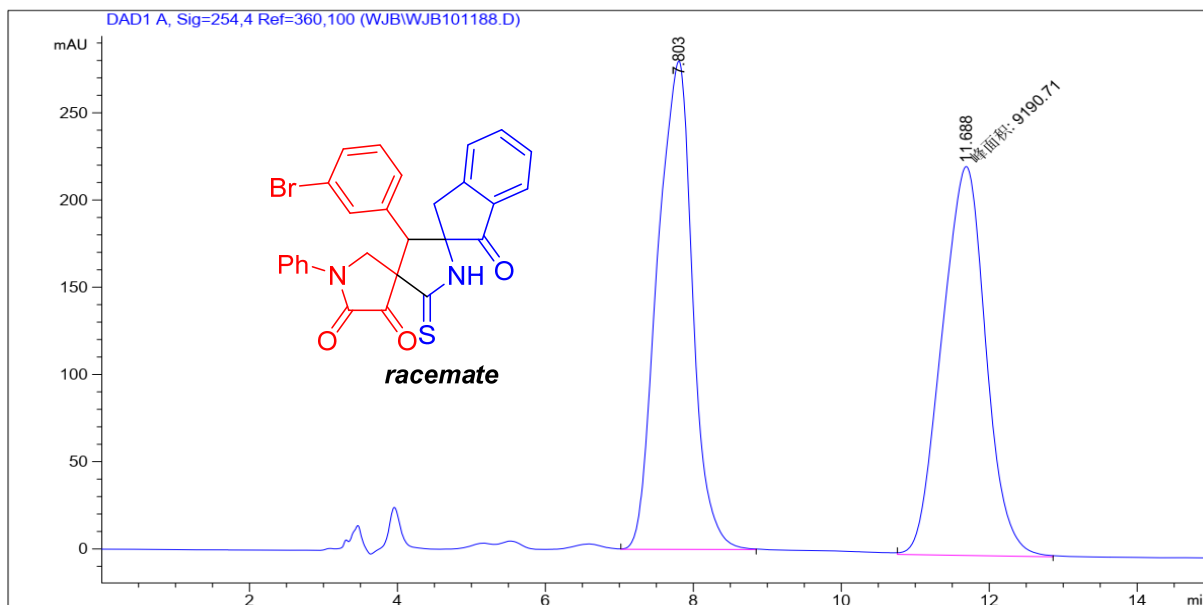
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.673	MM	2.2743	2.40706e4	176.39429	94.7680
2	41.415	MM	2.4729	1328.91638	8.95640	5.2320



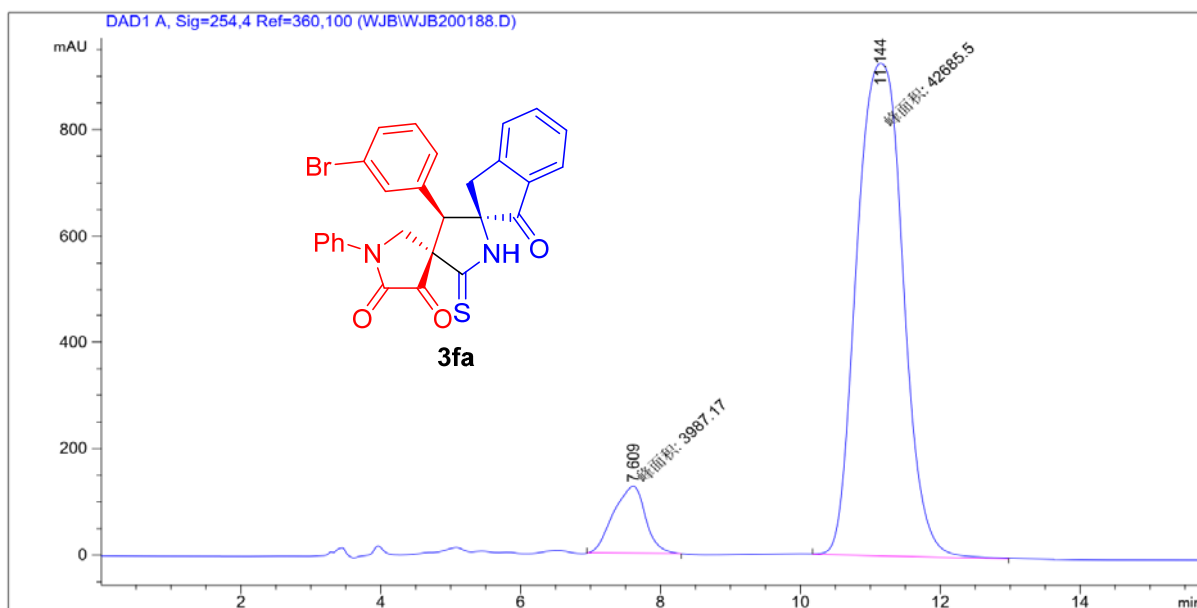
Peak #	Ret Time [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.577	VB	0.5445	2.09300e4	521.16418	50.0900
2	24.762	VB	1.1302	2.08548e4	280.23947	49.9100



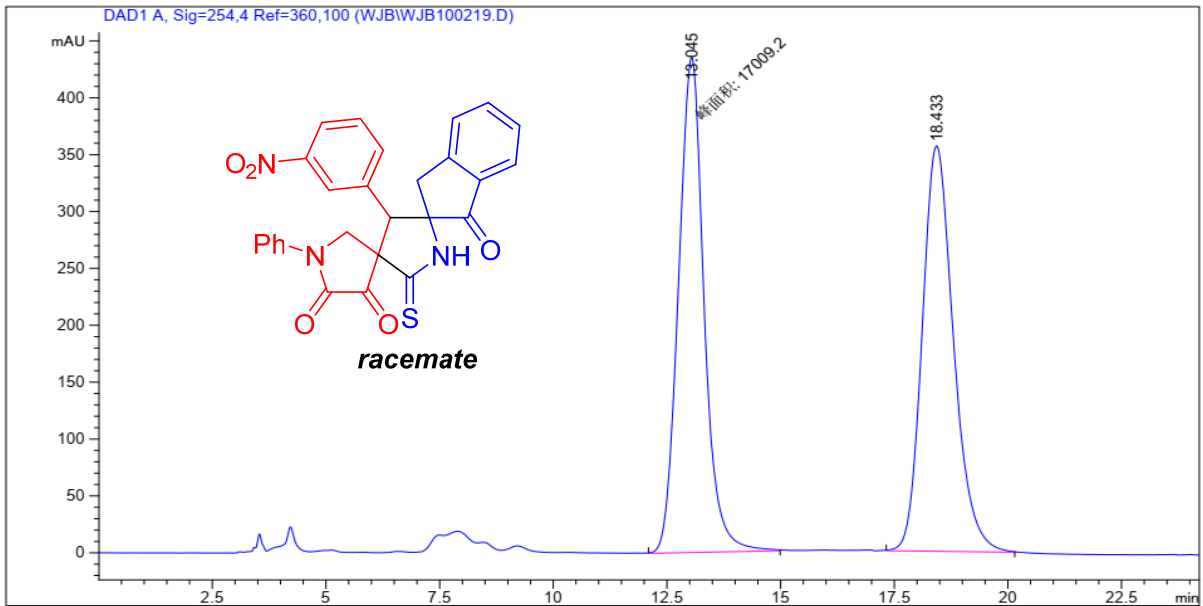
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.607	VV	0.3478	3137.69287	137.71315	5.5542
2	25.083	VB	1.0546	5.33549e4	758.54907	94.4458



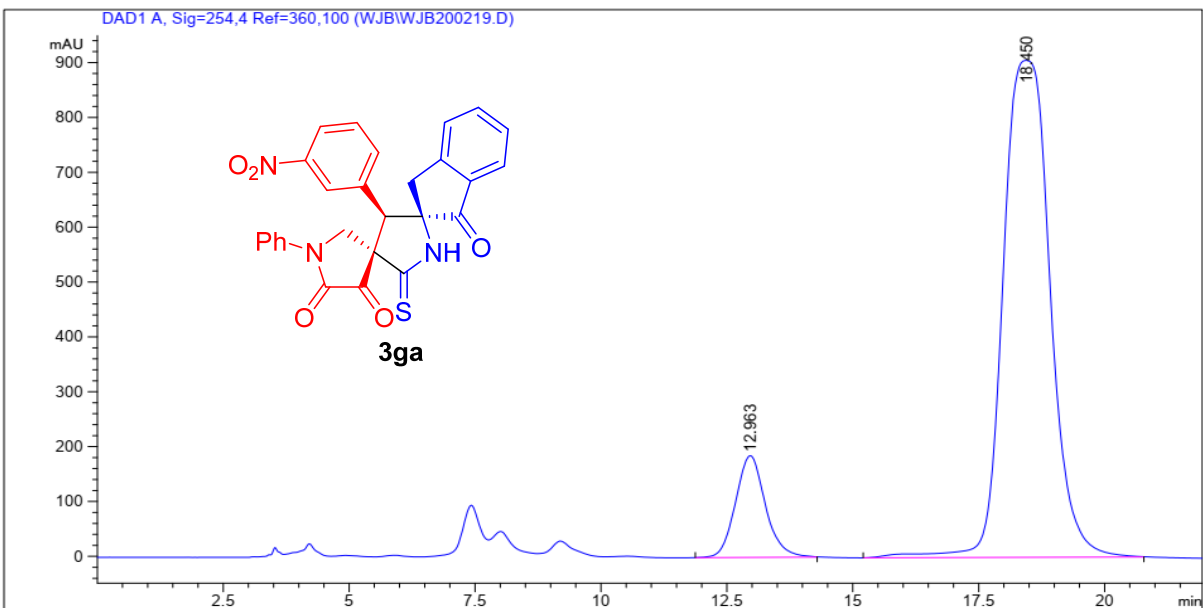
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.803	VB	0.5381	9214.88965	279.90295	50.0657
2	11.688	MM	0.6870	9190.71484	222.96318	49.9343



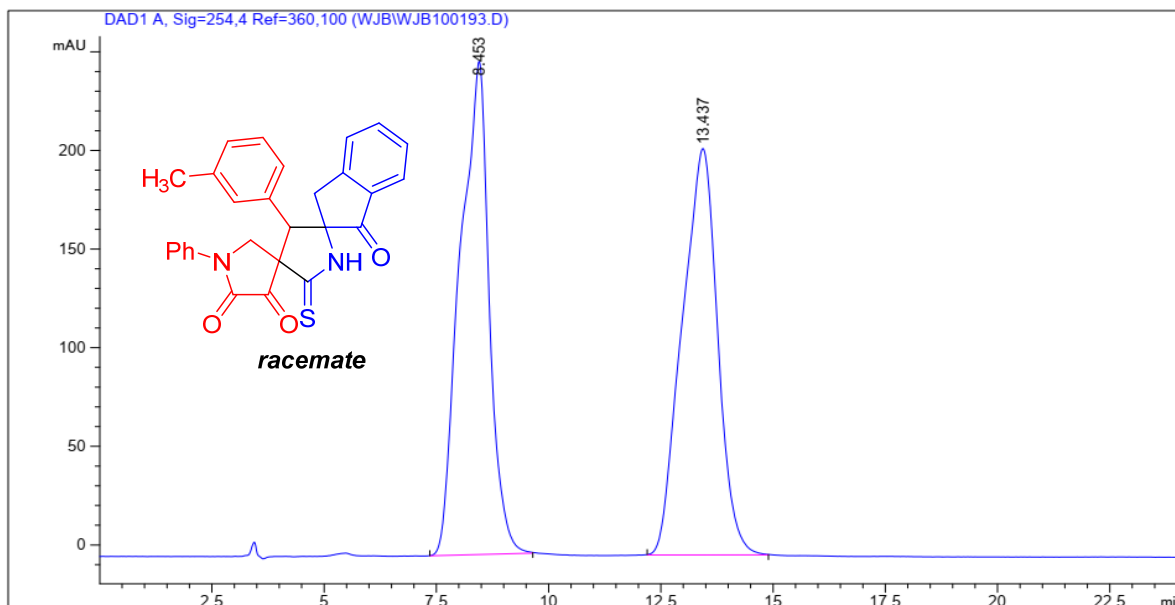
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.609	MM	0.5277	3987.16846	125.93576	8.5428
2	11.144	MM	0.7685	4.26855e4	925.79041	91.4572



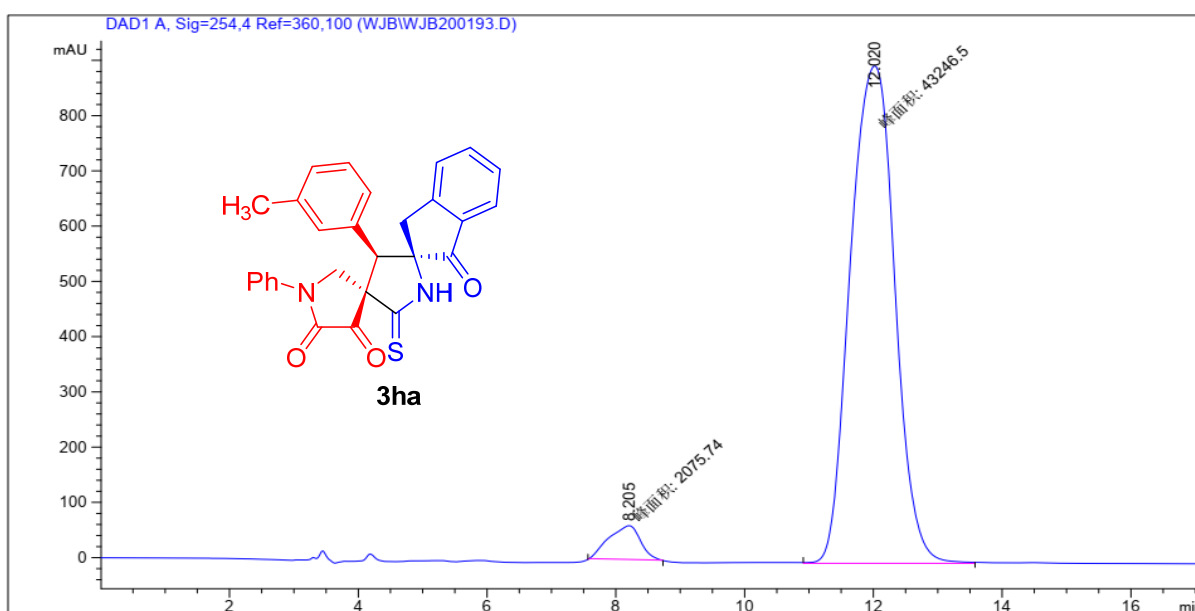
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.045	MM	0.6512	1.70092e4	435.32623	49.9898
2	18.433	BB	0.7351	1.70162e4	356.33008	50.0102



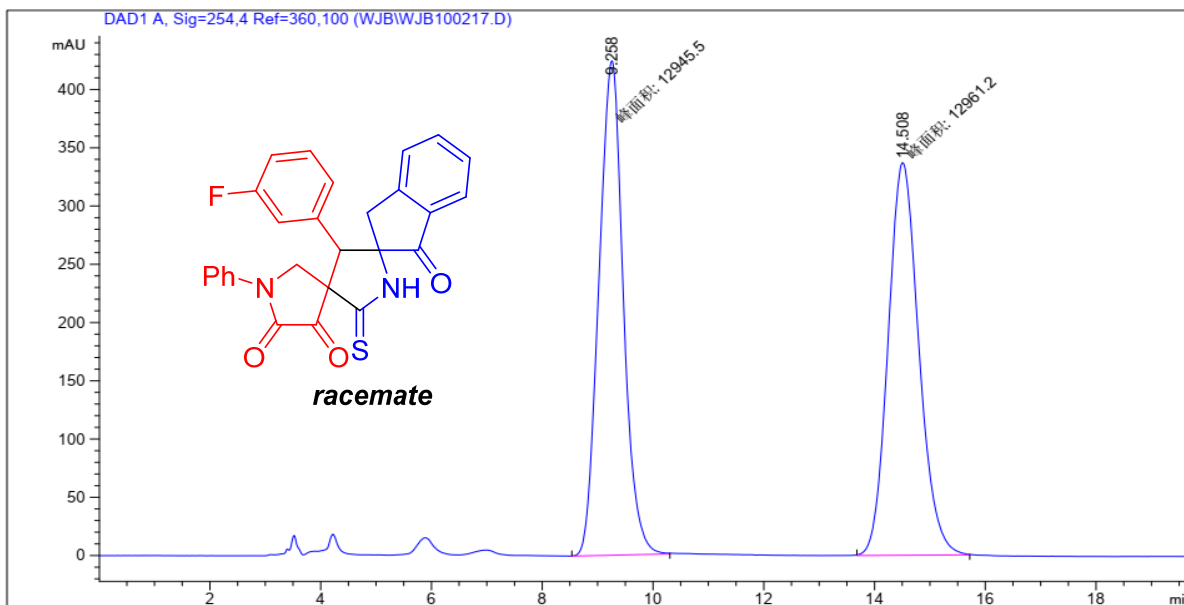
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.963	BB	0.6252	7652.33008	185.52492	11.5477
2	18.450	BB	0.7690	5.86149e4	905.77319	88.4523



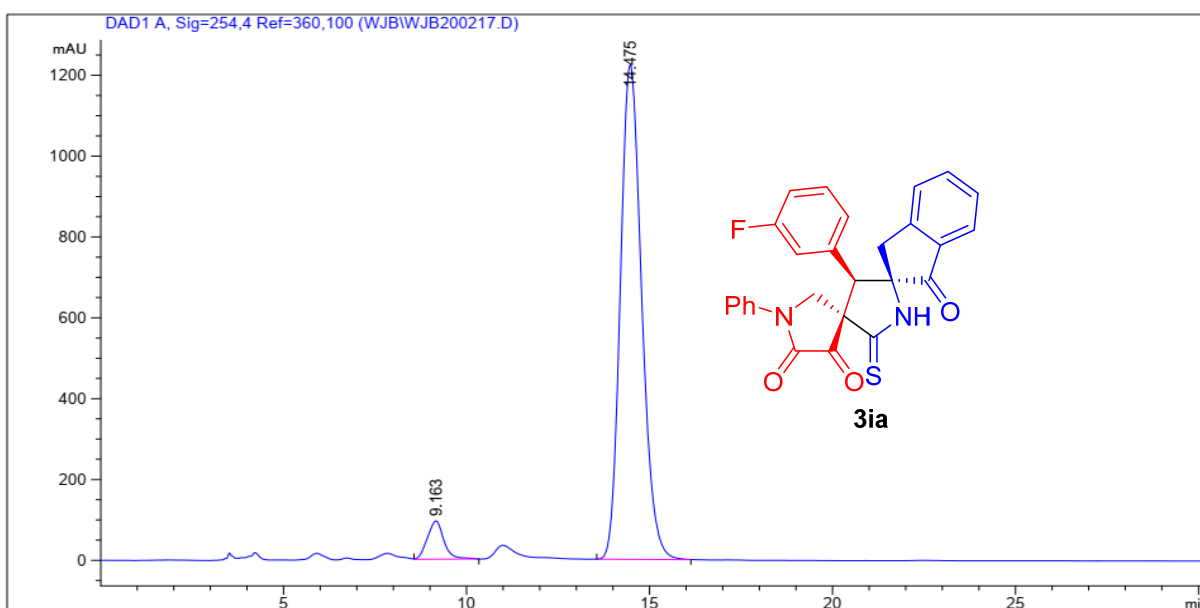
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.453	BB	0.6033	1.12569e4	250.02924	49.8972
2	13.437	BB	0.7761	1.13033e4	206.01018	50.1028



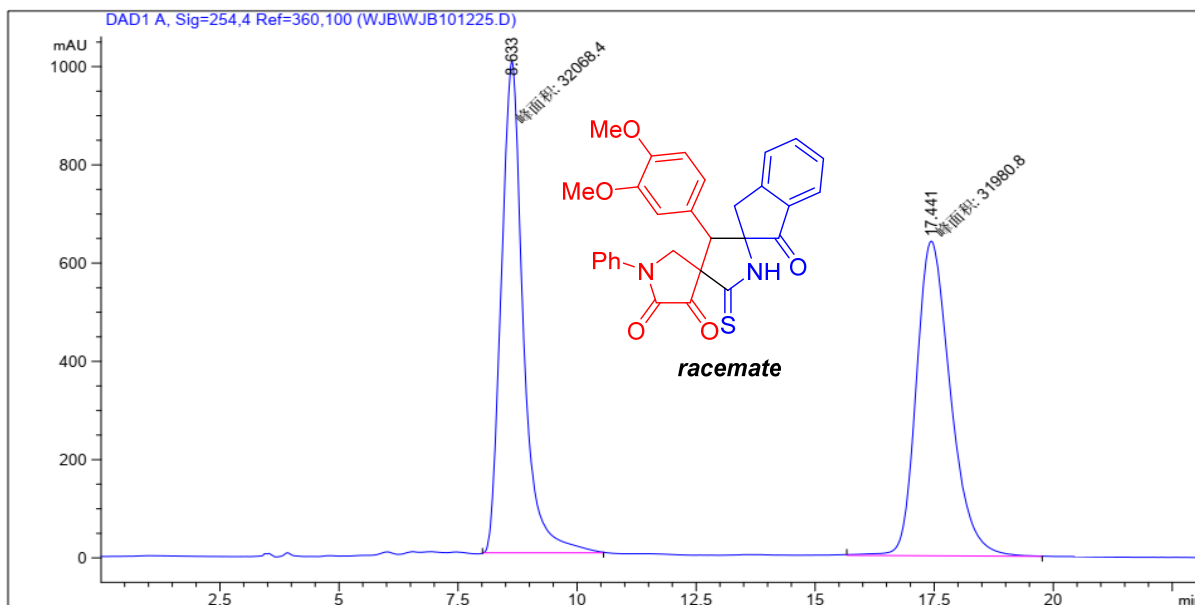
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.205	MM	0.5662	2075.73706	61.10561	4.5800
2	12.020	MM	0.8006	4.32465e4	900.29565	95.4200



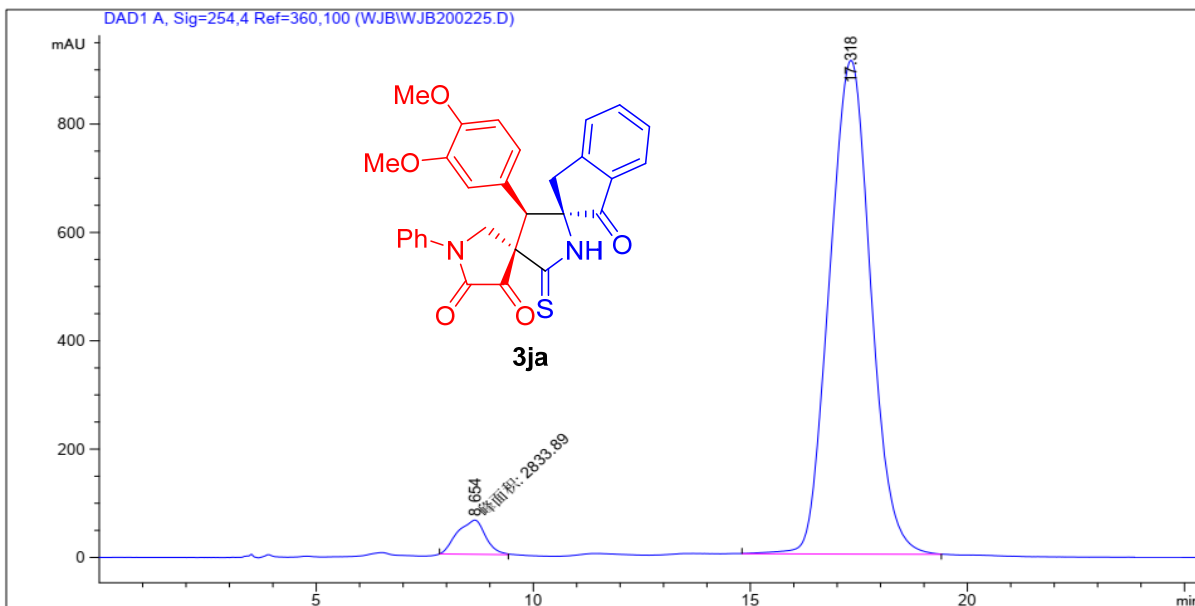
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.258	MM	0.5084	1.29455e4	424.35272	49.9697
2	14.508	MM	0.6412	1.29612e4	336.89322	50.0303



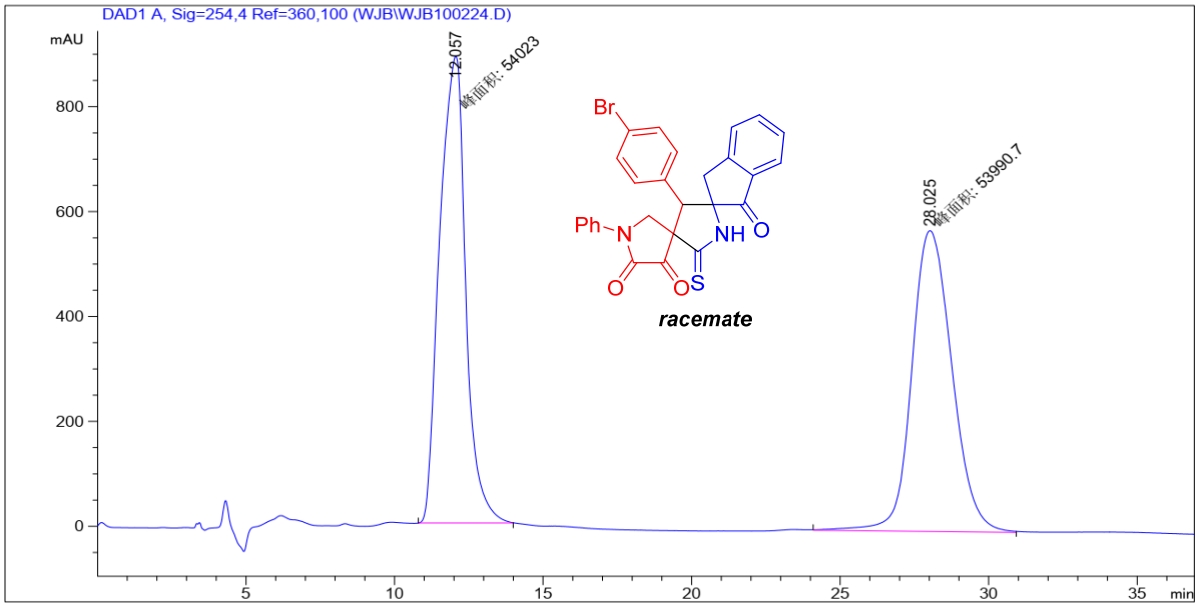
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.163	VB	0.4677	2966.26709	94.64110	5.6700
2	14.475	BB	0.6208	4.93485e4	1223.00525	94.3300



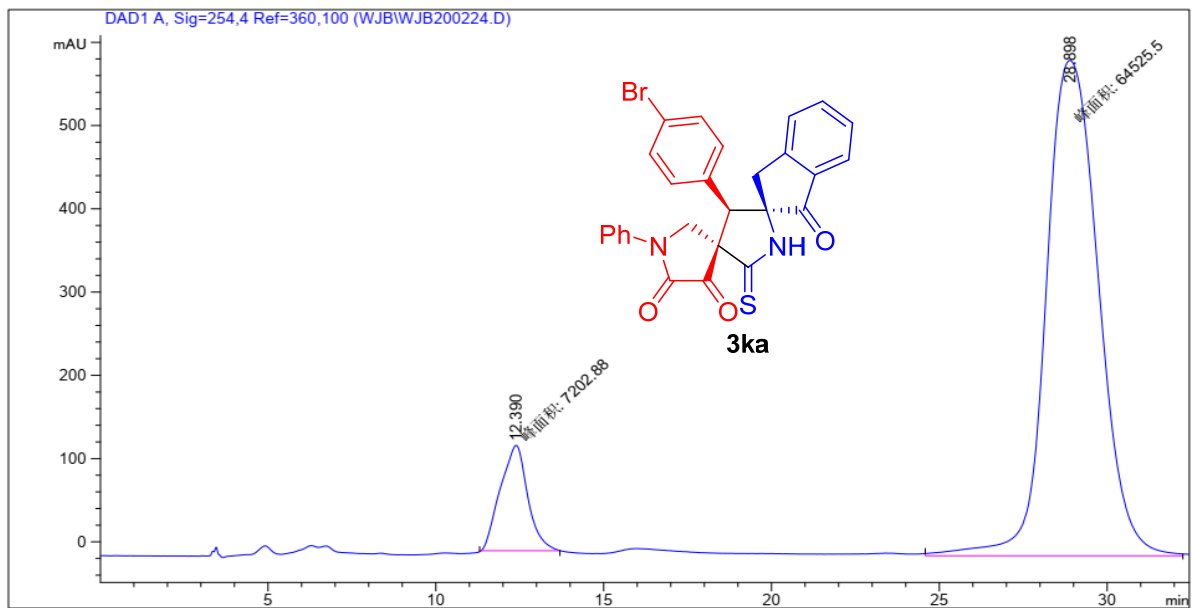
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.633	MM	0.5345	3.20684e4	1000.03088	50.0684
2	17.441	MM	0.8323	3.19808e4	640.41376	49.9316



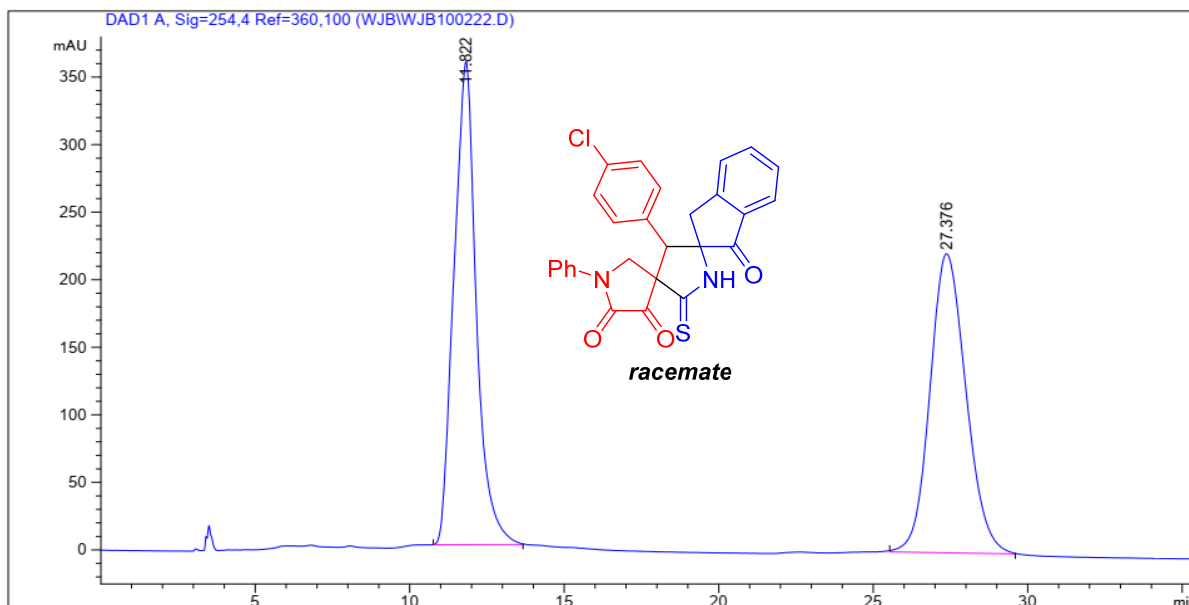
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.654	MM	0.7480	2833.88818	63.14351	4.4893
2	17.318	BB	0.8798	6.02910e4	911.33118	95.5107



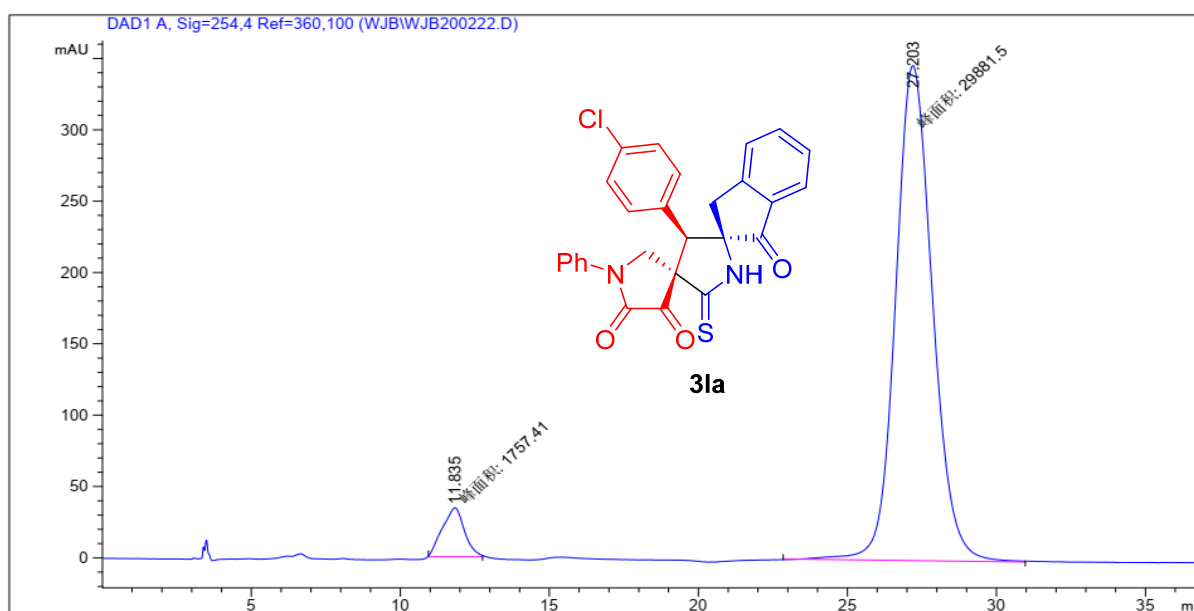
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.057	MM	1.0114	5.40230e4	890.22241	50.0149
2	28.025	MM	1.5690	5.39907e4	573.53198	49.9851



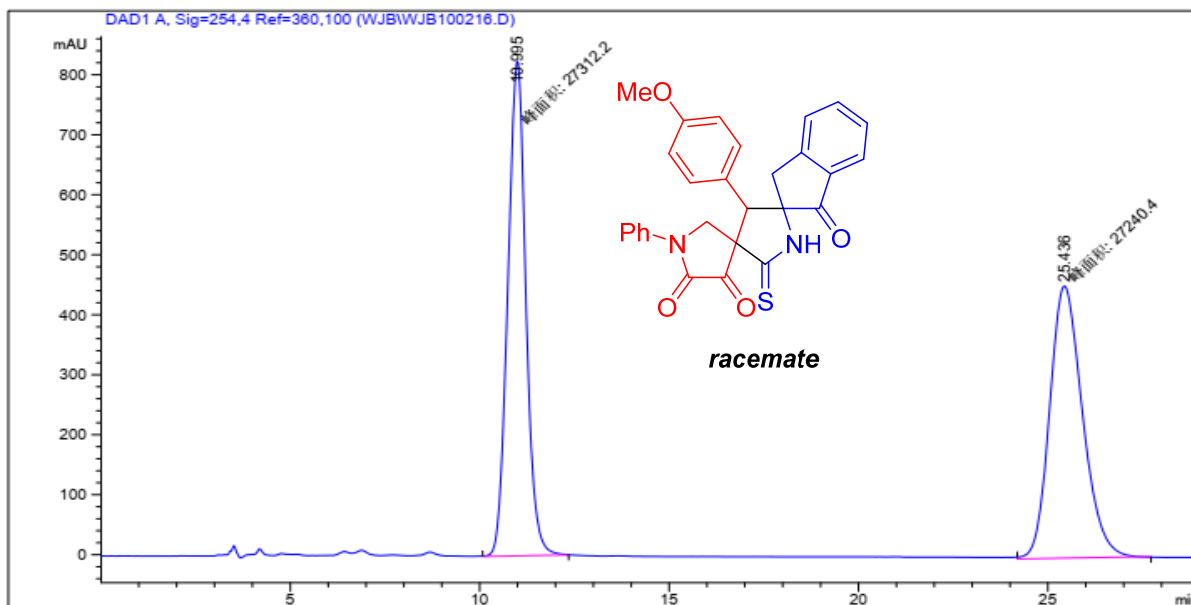
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.390	MM	0.9486	7202.88135	126.55871	10.0419
2	28.898	MM	1.8070	6.45255e4	595.15997	89.9581



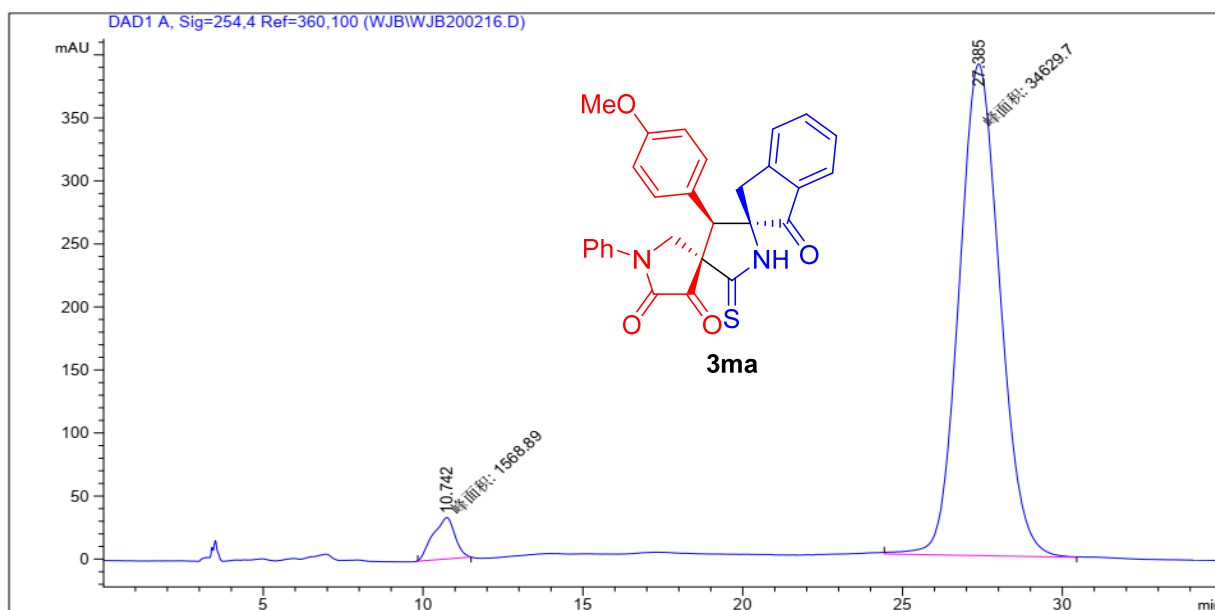
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.822	BB	0.7187	1.79832e4	357.61075	50.0750
2	27.376	BB	1.1352	1.79293e4	221.30309	49.9250



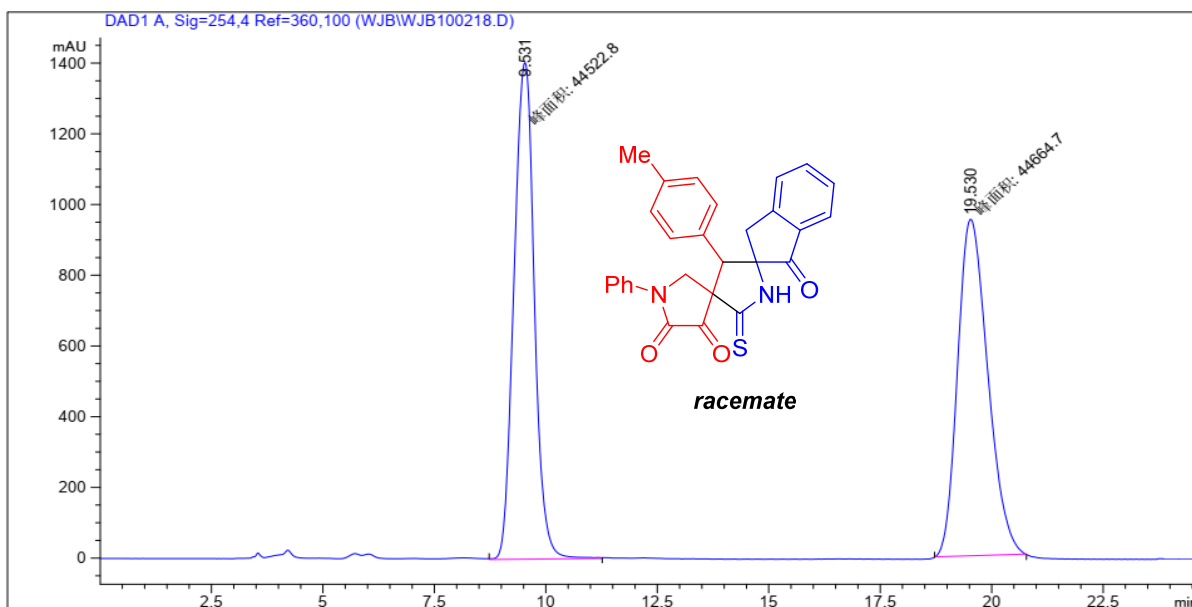
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.835	MM	0.8552	1757.40564	34.24881	5.5546
2	27.203	MM	1.4357	2.98815e4	346.88812	94.4454



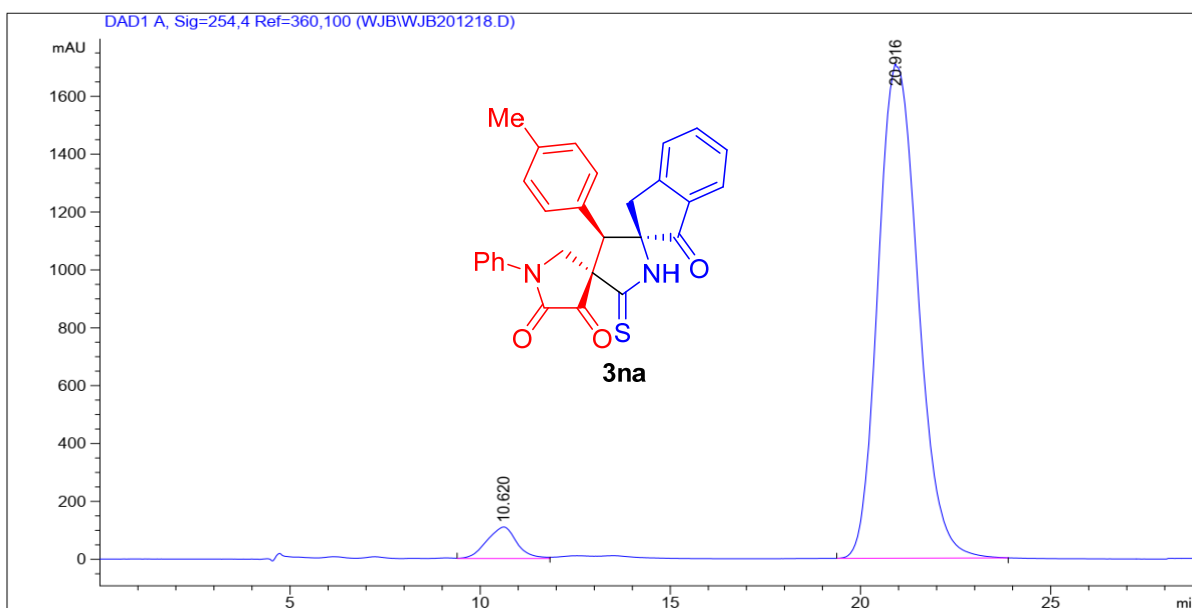
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.995	MM	0.5522	2.73122e4	824.37488	50.0657
2	25.436	MM	1.0010	2.72404e4	453.54199	49.9343



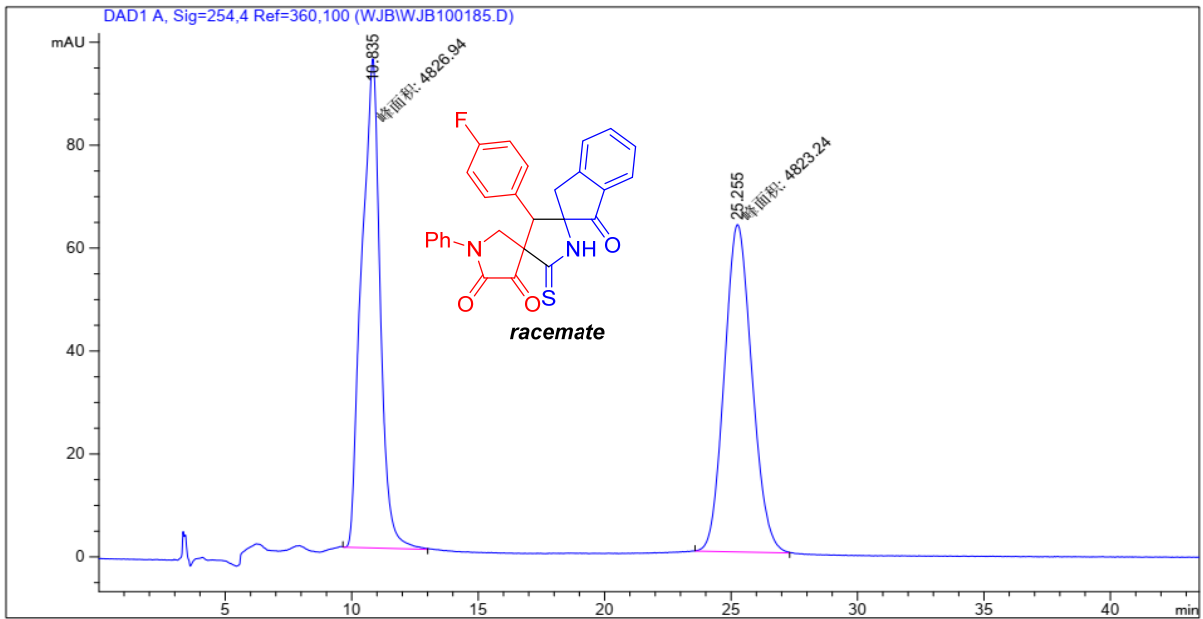
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.742	MM	0.7973	1568.88977	32.79636	4.3341
2	27.385	MM	1.4798	3.46297e4	390.03867	95.6659



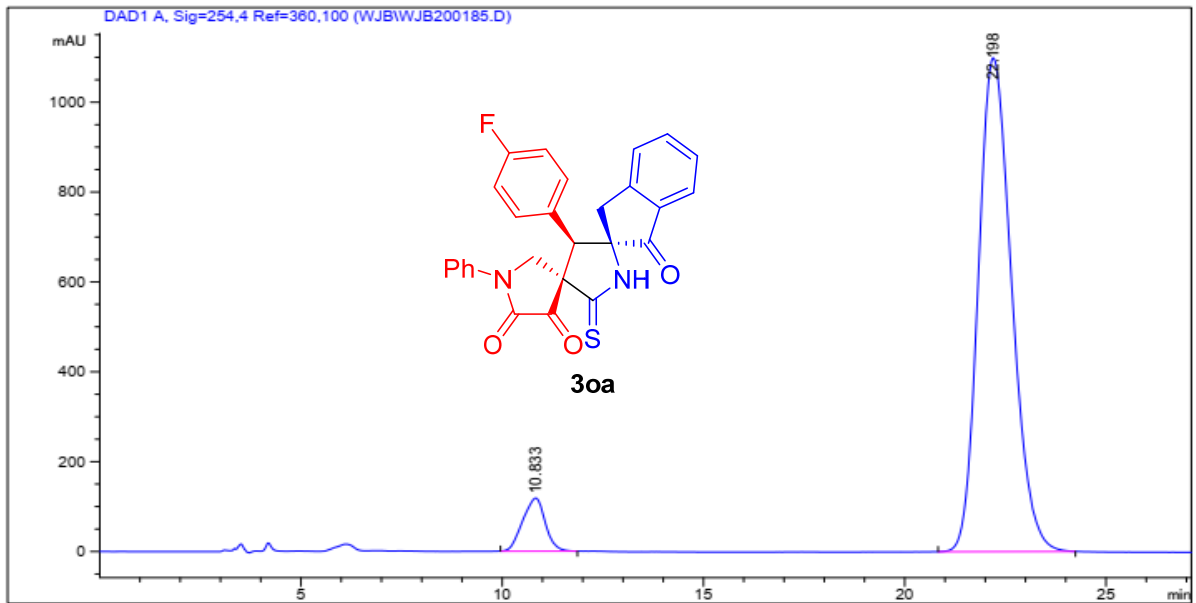
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.531	MM	0.5283	4.45228e4	1404.59973	49.9204
2	19.530	MM	0.7820	4.46647e4	951.92371	50.0796



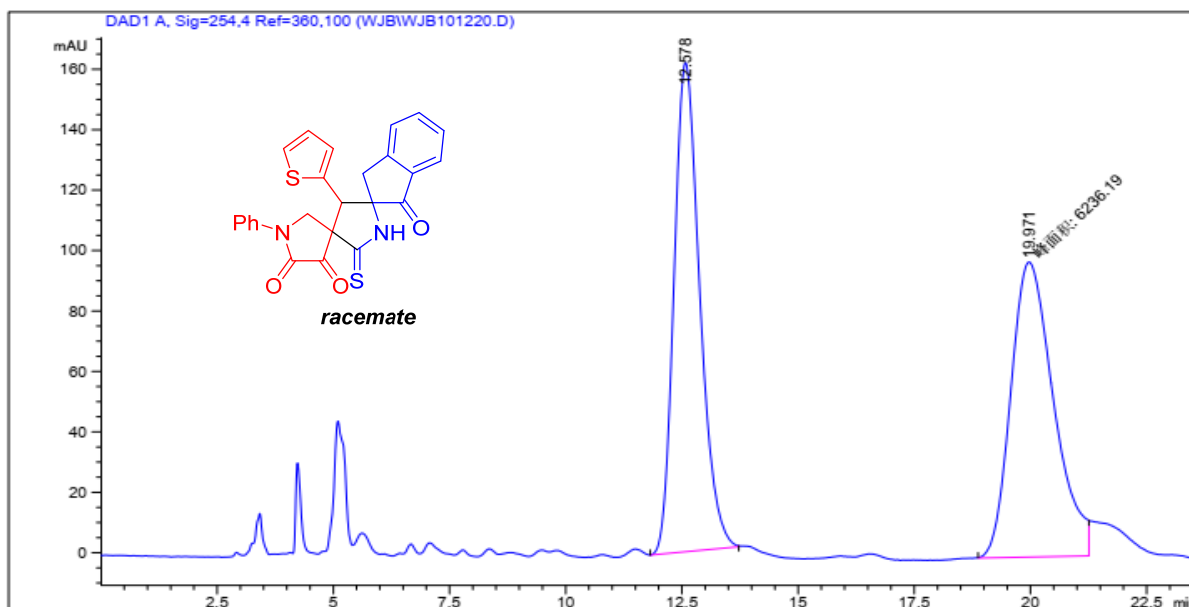
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.620	VV	0.7746	5979.69873	108.90514	4.5817
2	20.916	BB	0.8623	1.24532e5	1708.62732	95.4183



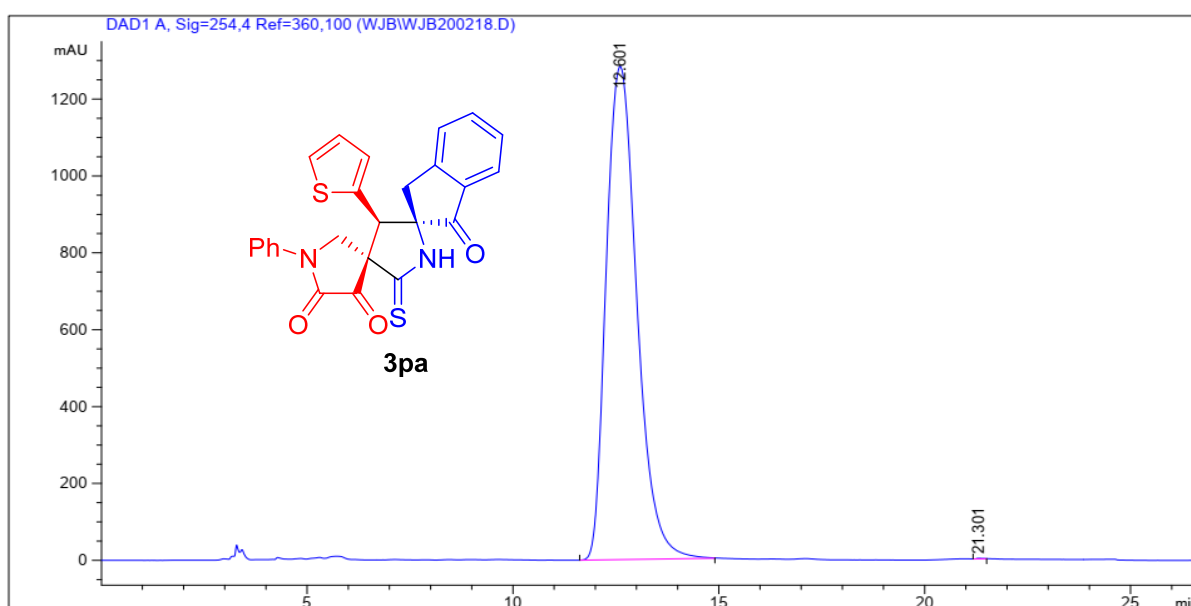
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.835	MM	0.8461	4826.94434	95.08164	50.0192
2	25.255	MM	1.2637	4823.23535	63.61287	49.9808



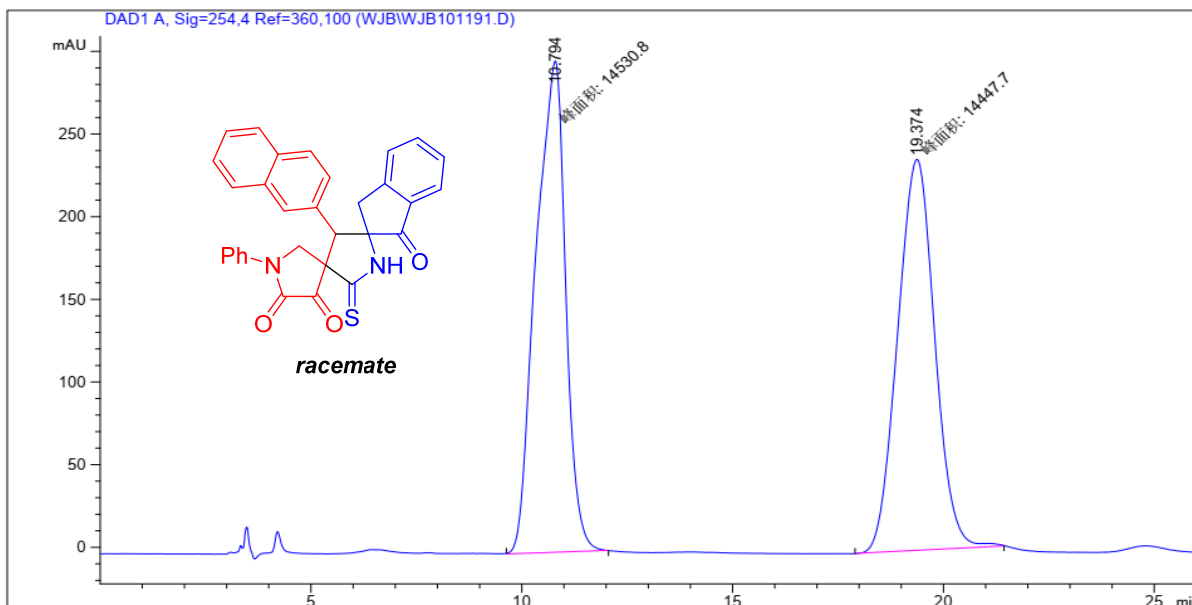
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.833	BB	0.5683	4602.51367	118.19185	6.8030
2	22.198	BB	0.8795	6.30518e4	1098.80945	93.1970



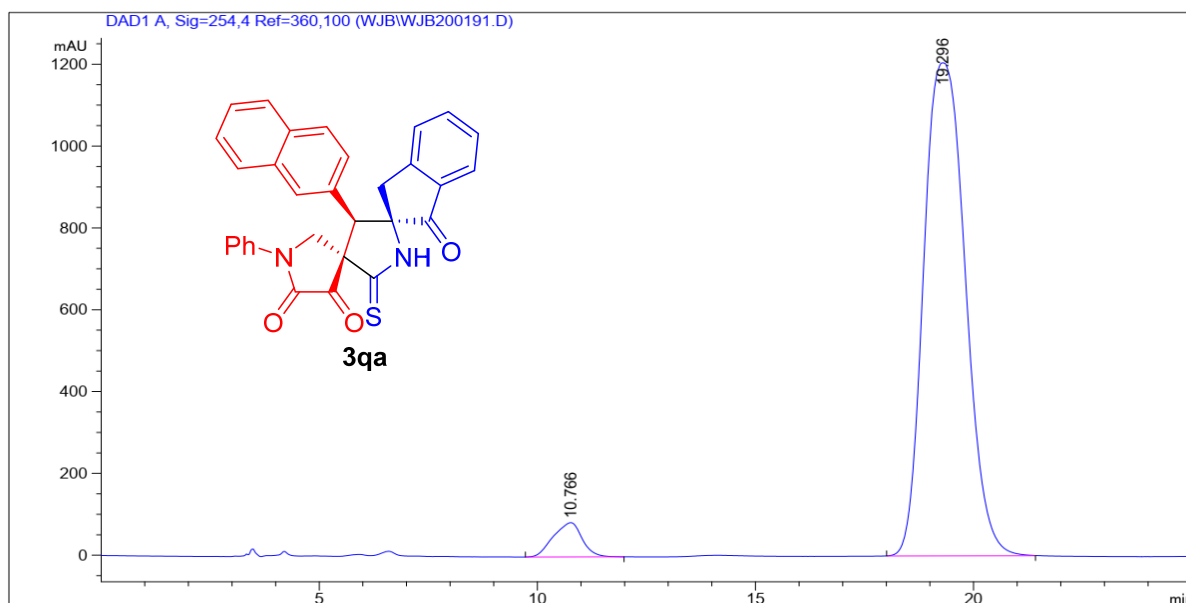
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.578	VB	0.5848	6225.21680	161.84186	49.9560
2	19.971	MF	1.0646	6236.19092	97.62936	50.0440



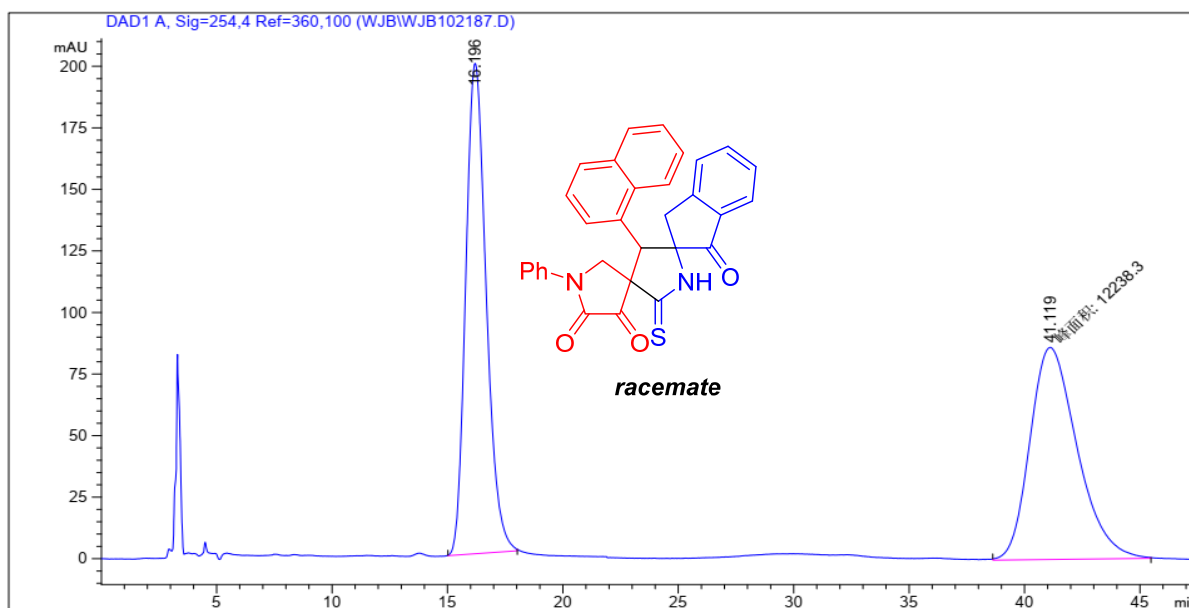
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.601	BB	0.8112	6.63796e4	1283.77661	99.9761
2	21.301	BB	0.1411	15.87580	1.45771	0.0239



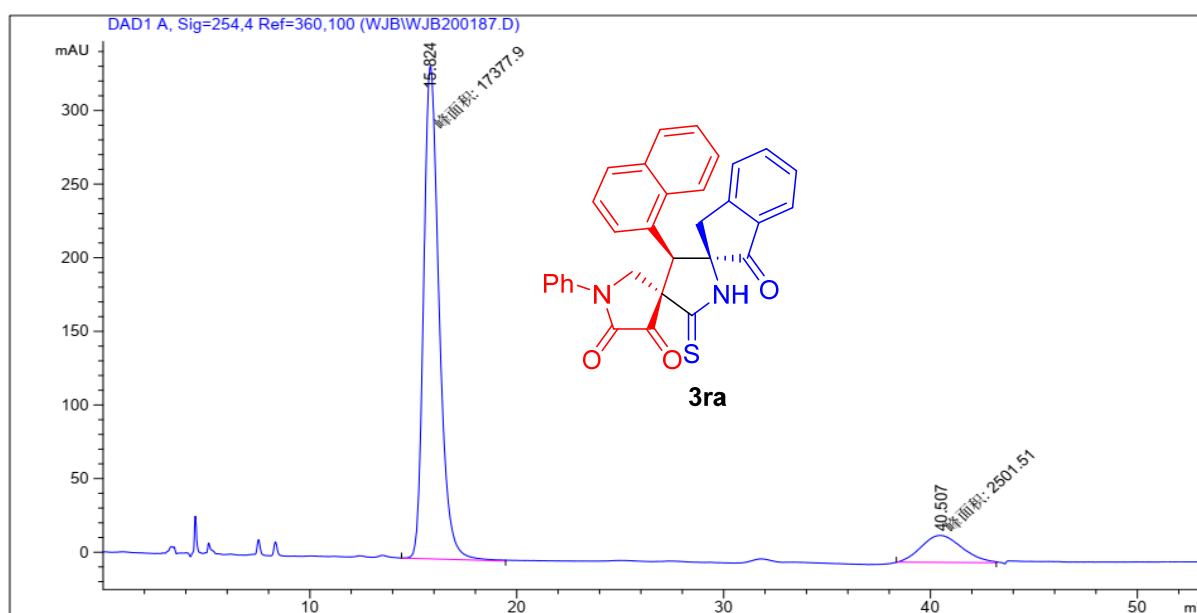
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.794	MM	0.8150	1.45308e4	297.13846	50.1434
2	19.374	MM	1.0180	1.44477e4	236.53587	49.8566



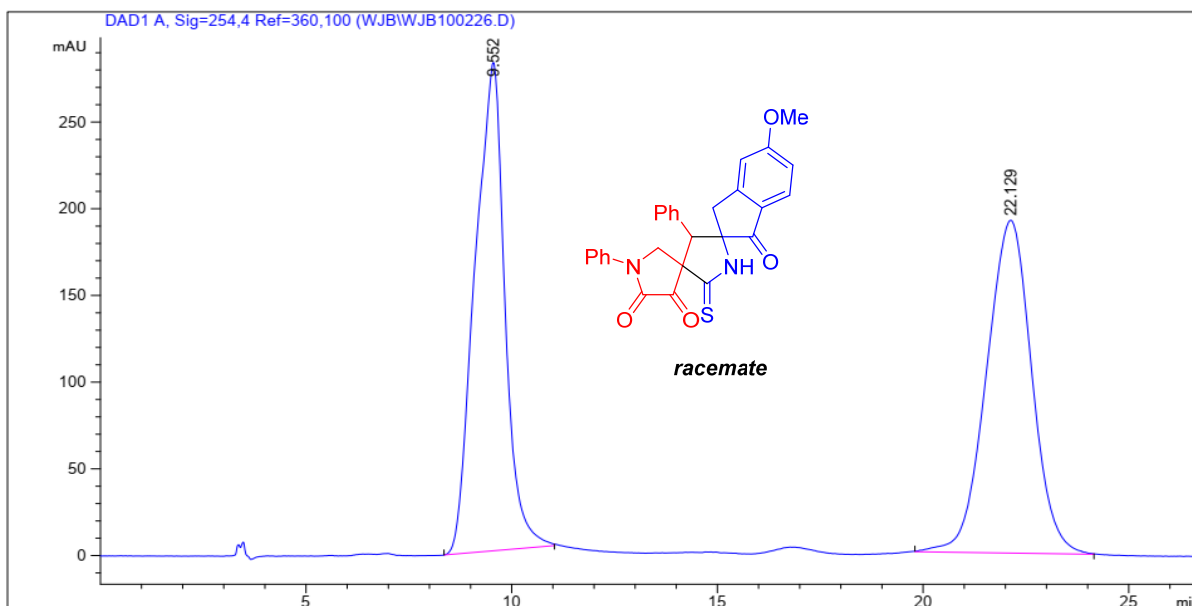
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.766	BB	0.6415	3844.32056	83.75391	4.5987
2	19.296	BB	0.7781	7.97523e4	1205.03979	95.4013



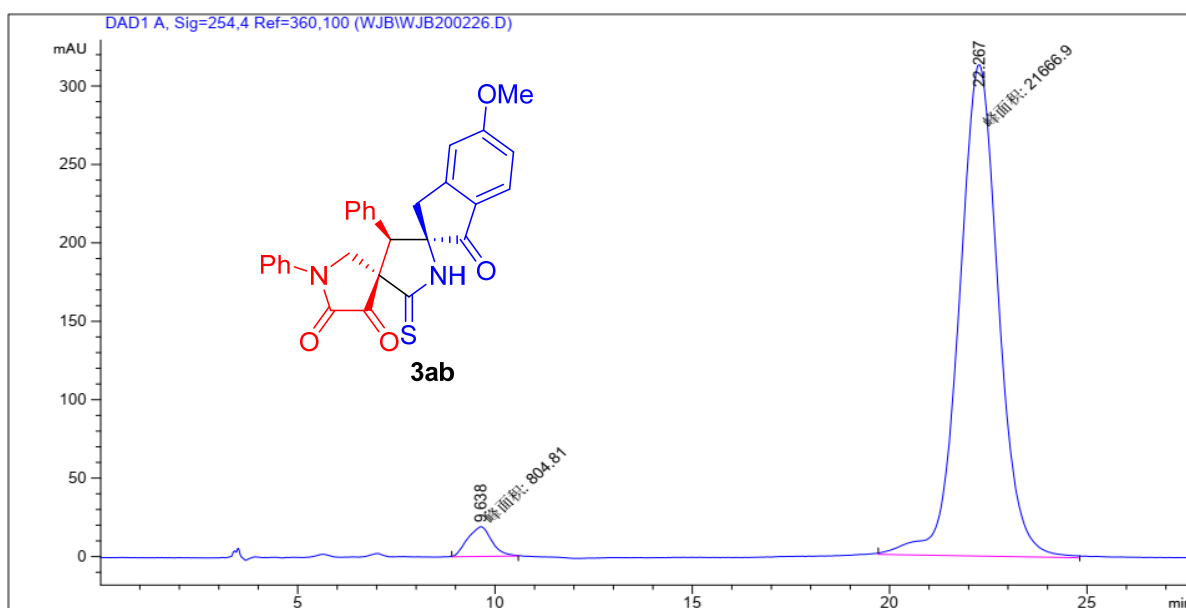
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.196	BB	0.9349	1.22392e4	199.18182	50.0019
2	41.119	MM	2.3672	1.22383e4	86.16573	49.9981



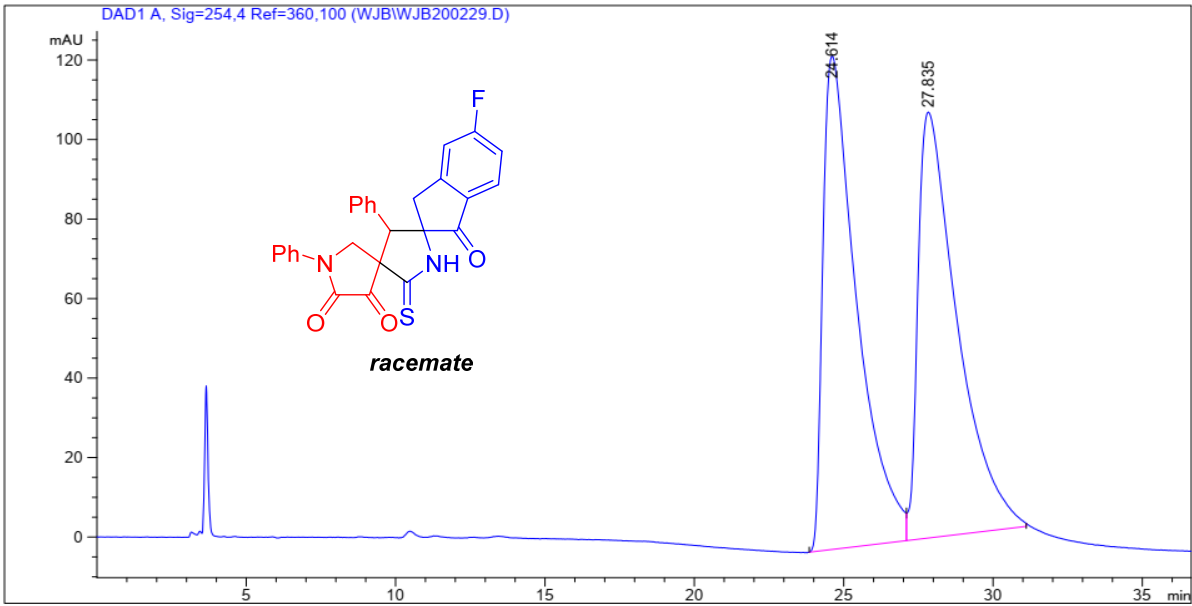
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	15.824	MM	0.8659	1.73779e4	334.48795	87.4165
2	40.507	MM	2.2765	2501.51392	18.31381	12.5835



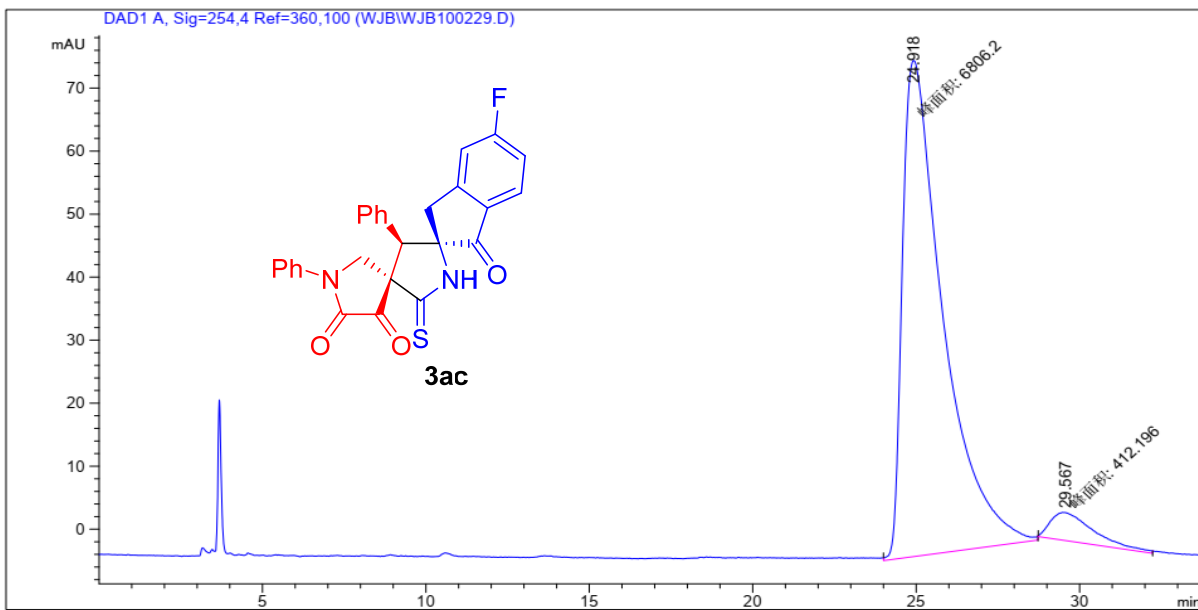
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.552	BB	0.6892	1.42222e4	281.61249	49.2431
2	22.129	BB	1.0673	1.46594e4	191.88948	50.7569



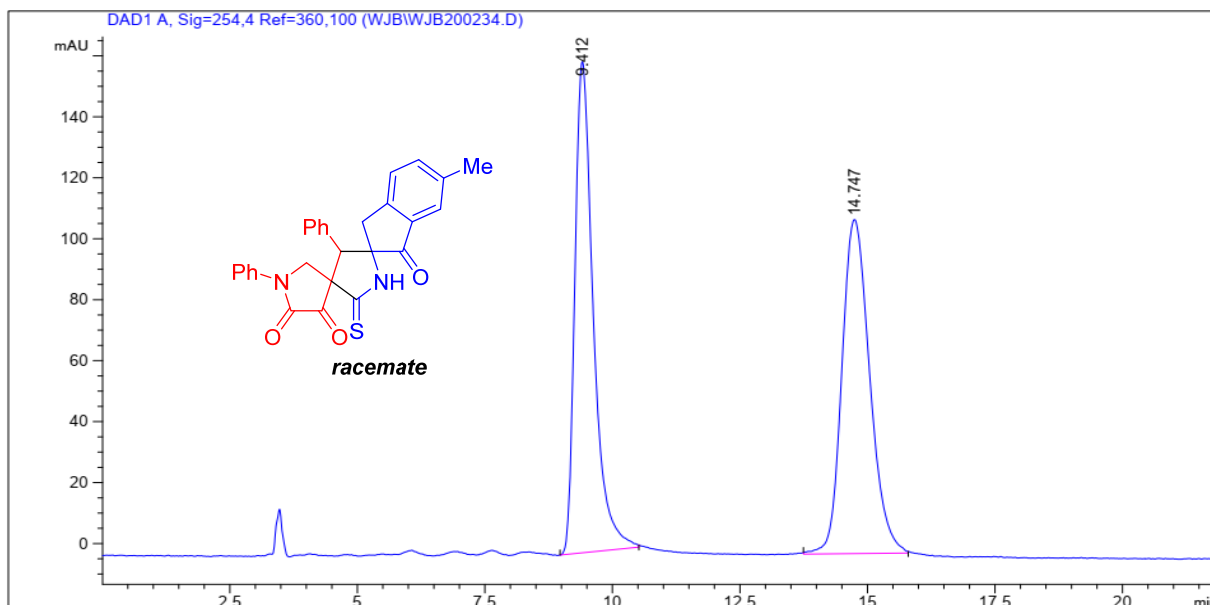
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.638	MM	0.7100	804.80969	18.89320	3.5814
2	22.267	MM	1.1528	2.16669e4	313.25269	96.4186



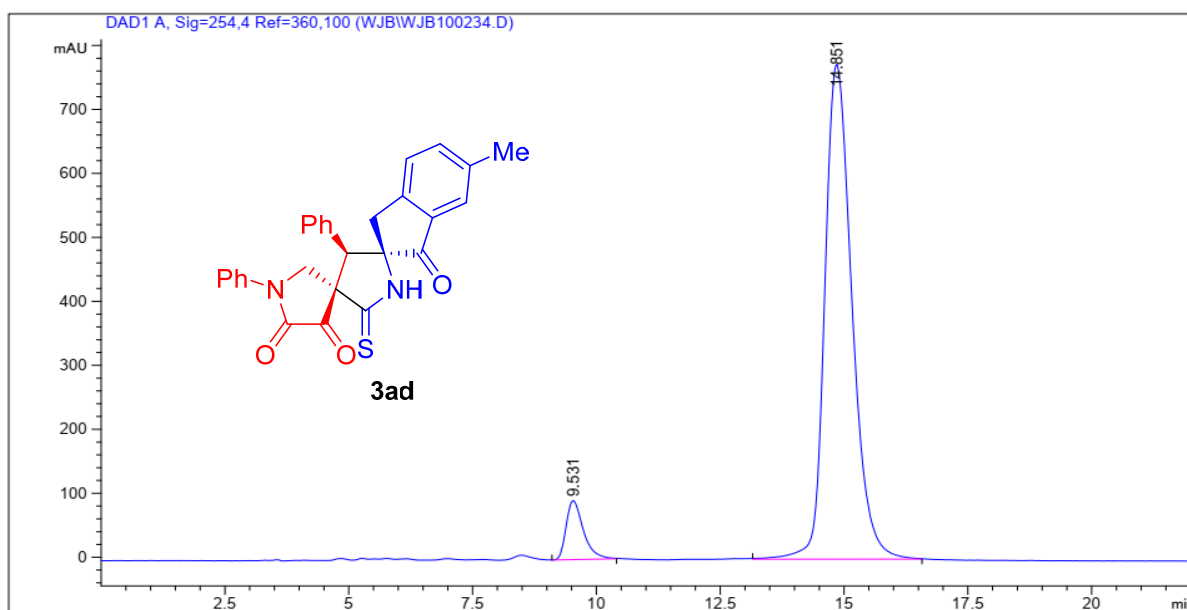
Peak #	Ret Time [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.614	BB	1.0924	9791.14648	124.10841	49.9833
2	27.835	BB	1.2128	9797.70801	107.14769	50.0167



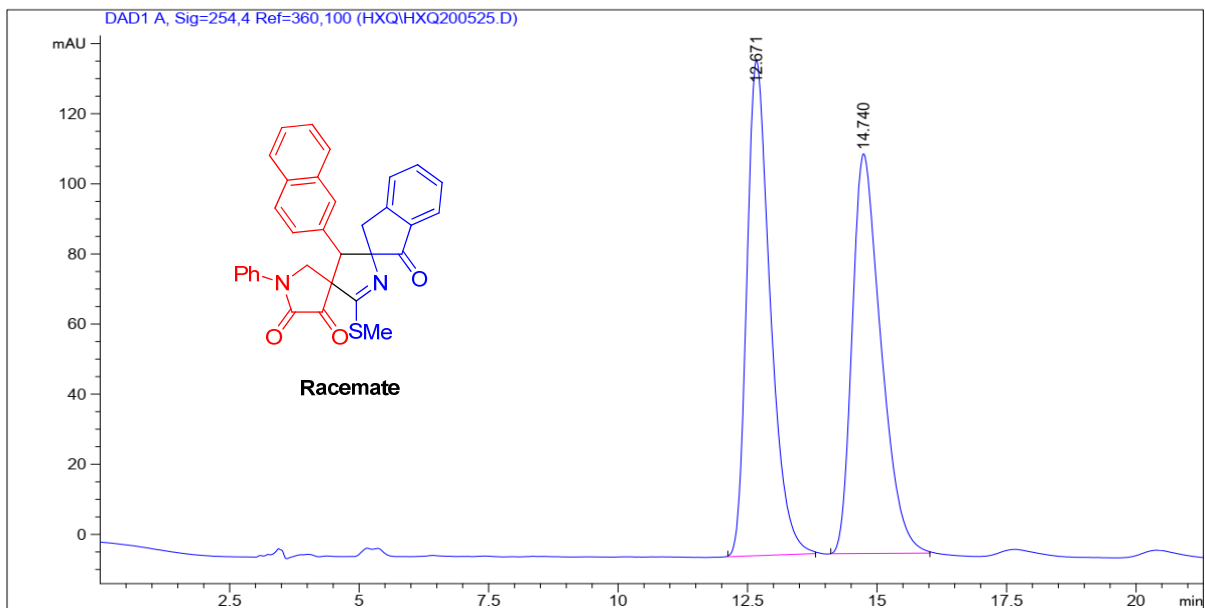
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.918	MM	1.4405	6806.19824	78.75037	94.2896
2	29.567	MM	1.5468	412.19559	4.44124	5.7104



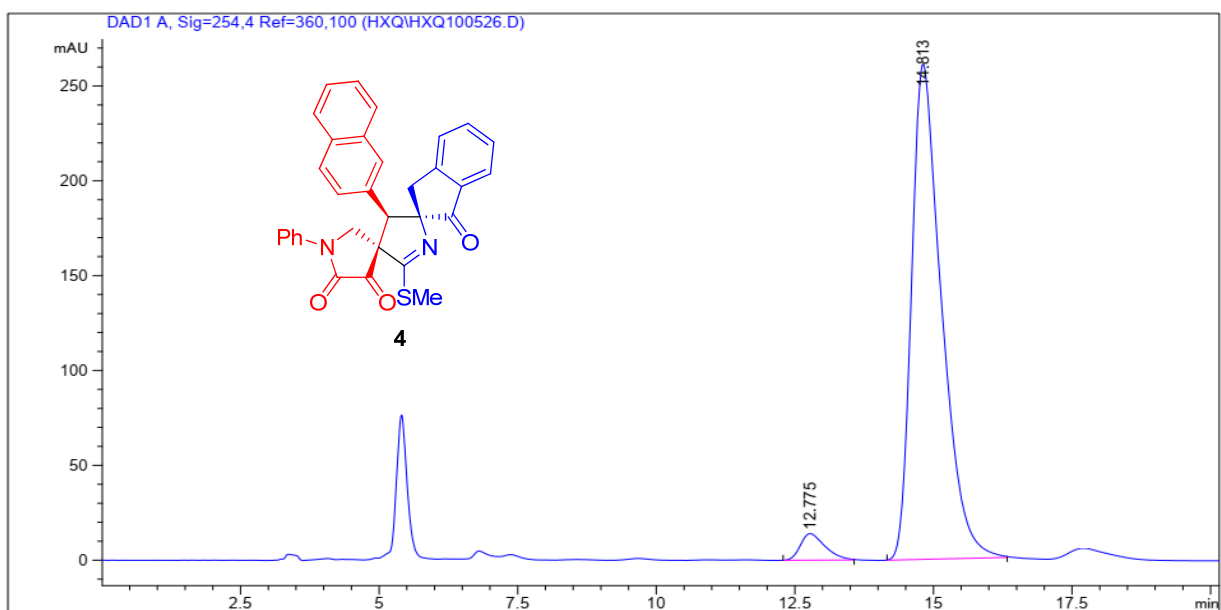
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.412	BB	0.3803	4036.21558	161.10580	49.2992
2	14.747	BB	0.5859	4150.96289	109.59423	50.7008



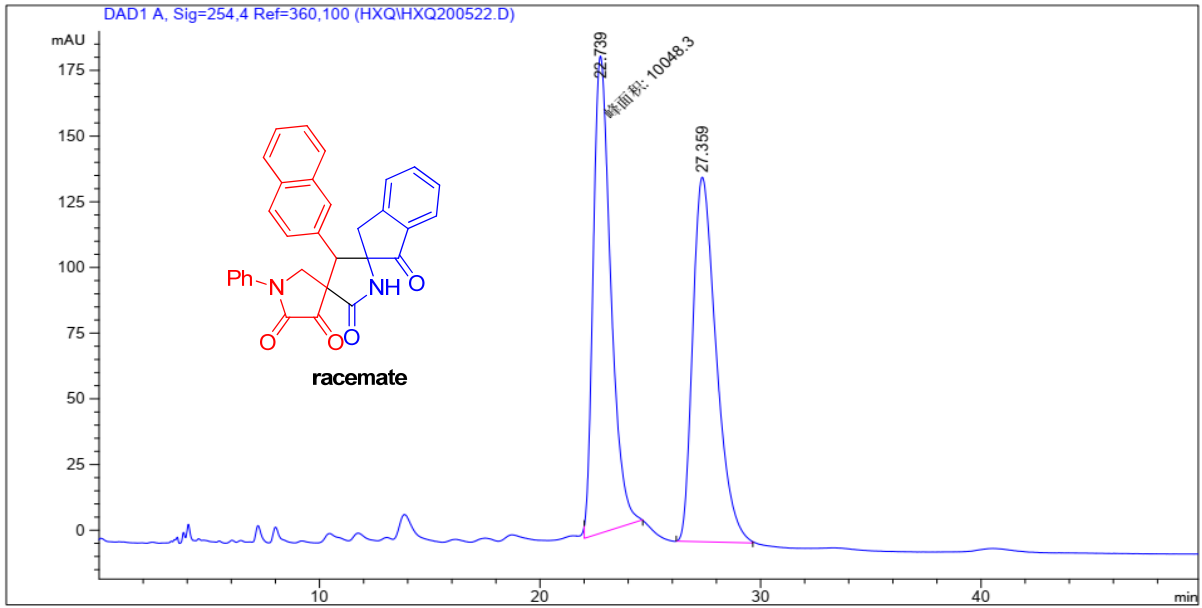
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.531	VB	0.3698	2225.45435	92.13474	7.0240
2	14.851	BB	0.5784	2.94582e4	773.42804	92.9760



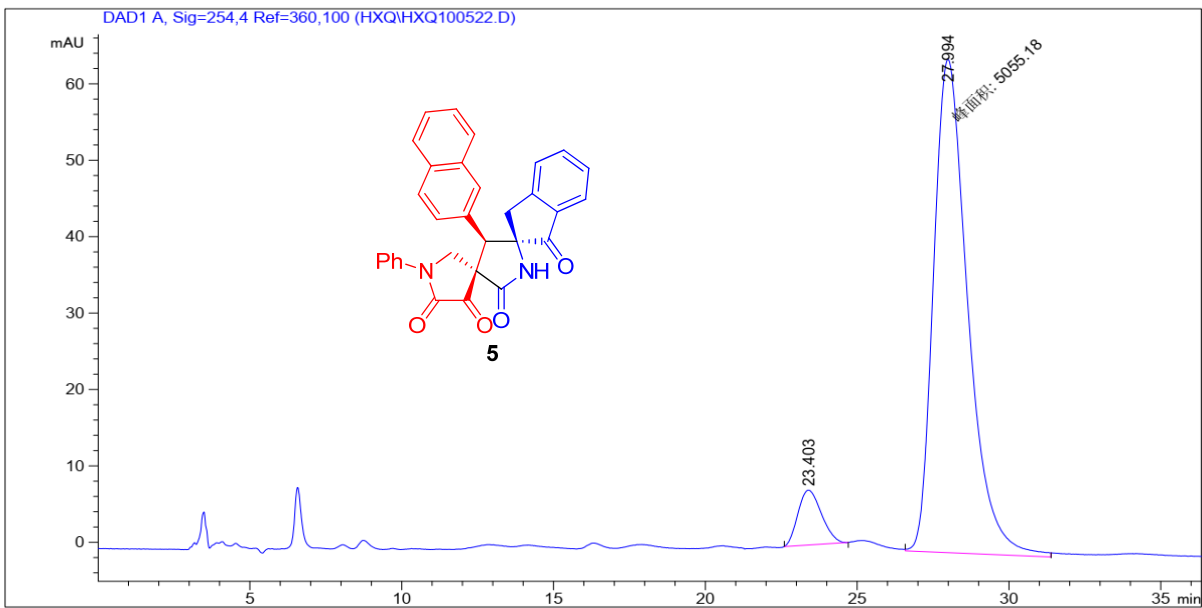
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.671	BB	0.4751	4445.34082	141.25862	50.2019
2	14.740	BB	0.5772	4409.58545	114.00653	49.7981



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.775	BB	0.4404	430.70996	14.02216	4.2048
2	14.813	BB	0.5505	9812.46289	261.08298	95.7952



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.739	MM	0.9222	1.00483e4	181.59441	49.4784
2	27.359	BB	1.1067	1.02601e4	138.75989	50.5216



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.403	BB	0.6504	384.94244	7.16922	7.0760
2	27.994	MM	1.3052	5055.17725	64.55166	92.9240