Organocatalytic enantioselective tandem sulfa-Michael/aldol reaction to access dihydrothiopyran-fused benzosulfolane skeletons bearing three contiguous stereocenters

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Supporting Information

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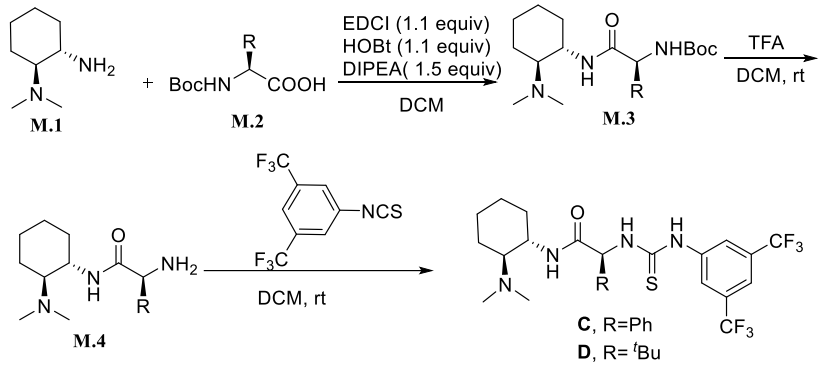
1. General Information

Reagents were purchased from commercial sources and were used as received unless mentioned otherwise. Reactions were monitored by TLC. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ and DMSO-d_6. ^{1}H NMR chemical shifts are reported in ppm relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$ at 7.26 ppm, DMSO-d_6 at 2.50 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$ at 77.20 ppm, DMSO-d_6 at 39.51 ppm). Melting points were recorded on a melting point apparatus.

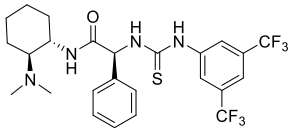
2. Catalyst synthesis.[1]



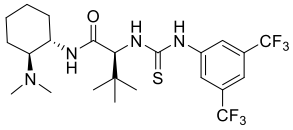
To a round bottomed flask equipped with a magnetic stirring bar was added EDCI (27.84 mmol, 1.1 equiv), HOBT (27.84 mmol, 1.1 equiv.), CH_2Cl_2 (DCM) (50 mL) and DIPEA (34.8 mmol, 1.1 equiv.) via syring. After short stirring, and then compound **M.1** was added to the mixture, followed by slow addition of compound **M.2**. The mixture was stirred at room temperature until the reaction was complete monitored by TLC. Then 30 mL water was added to the mixture and the aqueous phase extracted with DCM (50 mL x 3). The combined organic phases were washed with brine, dried by Na_2SO_4, and concentrated under reduced pressure. The residue purified by flash chromatography to afford the desired product **M.3** (5.94 g, 72% yield).

Compound **M.3** (15 mmol, 1.0 equiv) was dissolved in DCM (20 mL), cooled to 0 ℃ and trifluoroacetic acid (150.0 mmol, 10.0 eq.) in DCM (10) was added dropwise. After 10 mins, the reaction temperature was allowed to warm up to room temperature and stirred overnight. The mixture was cooled to 0 ℃, then 1M NaOH was added to it until the pH to 12. Then the resulting mixture was extracted with DCM (50 mL x 3), the combined organic phase washed with brine and dried by Na_2SO_4, filtered, concentrated under reduced pressure to afford the crude product **M.4**.

The crude product **M.4** was dissolved in DCM (20.0 mL) at room temperature and the 3,5-bis(trifluoromethyl)phenyl isothiocyanate (2.4 mmol, 1.1 equiv.) was added dropwise via funnel at 0 ℃. After 10 mins, the reaction temperature was allowed to warm up to room temperature, and the mixture was stirred at room temperature. After 30 min, the solvent was removed and the residue purified by flash chromatography to afford catalysts **C**, **D** as a white solid.



(*S*)-2-(3-(3,5-*bis*(trifluoromethyl)phenyl)thioureido)-*N*-((1*S*,2*S*)-2-(dimethylamino)cyclohexyl)-2-phenylacetamide (C): white solid; yield 97%; $[\alpha]_D^{20}$ = +41.9 (*c* 1.0, CH_2Cl_2); m.p.216.4-217.3 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.42 (s, 1H), 8.70 (s, 1H), 8.05 (s, 2H), 7.51 (s, 1H), 7.29 (q, *J* = 4.8, 3.3 Hz, 5H), 6.76 (s, 1H), 6.20 (s, 1H), 3.36 (s, 1H), 2.35 (d, *J* = 12.9 Hz, 1H), 2.22 (s, 1H), 1.96 (s, 6H), 1.76 (t, *J* = 10.2 Hz, 2H), 1.58 (d, *J* = 11.7 Hz, 1H), 1.37-0.94 (m, 4H). 13C NMR (75 MHz, CDCl3) δ 181.4, 172.4, 140.7, 136.5, δ 131.50 (q, J = 33.4 Hz), 129.1, 128.7, 128.6, 127.7, 125.1, 123.3, 121.5, 117.8, 66.5, 62.1, 52.3, 39.6, 32.5, 25.1, 24.5, 21.4. HRMS (ESI) Calcd. for C25H29F6N4OS, $[M+H]^+$ 547.1961; found: 547.1980.



(*S*)-2-(3-(3,5-*bis*(trifluoromethyl)phenyl)thioureido)-*N*-((1*S*,2*S*)-2-(dimethylamino)cyclohexyl)-3,3-dimethylbutanamide (D): white solid; yield 95%; $[\alpha]_D^{20}$ = -5.8 (*c* 1.0, CH_2Cl_2); m.p.212.3-213.5 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.17 (s, 1H), 7.94 (s, 2H), 7.55 (s, 1H), 6.46 (d, *J* = 5.1 Hz, 1H), 5.04 (s, 1H), 3.51 (d, *J* = 4.9 Hz, 1H), 2.20 (s, 8H), 1.84 (d, *J* = 9.4 Hz, 1H), 1.75 (d, *J* = 8.1 Hz, 1H), 1.51 (d, *J* = 10.6 Hz, 1H), 1.12 (s, 13H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.0, 172.3, 140.5, δ 131.6 (q, J = 33.5 Hz), 128.7, 125.1, 124.2, 124.2, 121.5, 118.3, 117.8, 66.8, 66.7, 52.0, 40.1, 35.3, 32.6, 27.4, 25.1, 24.6, 21.2. HRMS (ESI) Calcd. for $C_{23}H_{33}F_6N_4OS$ $[M+H]^+$ 527.2274, found: 527.2286.

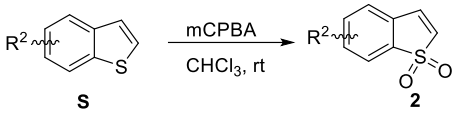
3. General procedure for the preparation of substrates 1. [2,3]

To a mixture of DMF (5 equiv., 20 mL) and $CHCl_3$ (10 mL) was added $POCl_3$ (2.5 equiv., 20 mL) via a funnel drop by drop over 20 mins at 0 ºC. After 30 mins, a mixture of oxindole **S1** (R^1 = H) (6.4 g 48 mmol), pyridine (0.2 equiv, 10 mL) and $CHCl_3$ (50 mL) was added via a funnel at 0 ºC. The mixture was stirred overnight at room temperature. The mixture was poured in to ice-cold H_2O and the solid compounds was filtered and dried. The crude product **M1**was obtained (6.9 g, 80% yield).

The crude product **M1** (R^1 = H) (5 g 27.84 mmol) was dissolved in 50 mL DCM, and the Boc_2O (29.23 mmol, 1.05 equiv.) was added dropwise via funnel at 0 ℃ and the reaction temperature was allowed to warm up to room temperature, and the mixture was stirred at room temperature until the reaction was complete monitored by TLC. The mixture was concentrated under reduced pressure. The residue purified by flash chromatography to afford the desired product **M2** (9.5 g 82%yield).

The above product **M2** (R^1 = H) (4g, 14.28 mmol) was dissolved in methanol (20 mL), the sodium hydrogensulfide hydrate (1.77 g, 1.5 equiv.) was added. After stirring for 3 h at room temperature the reaction mixture was poured into water. Then 1 M HCl was added to it until the pH to 1~2. Then the resulting mixture was extracted with DCM (30 mL x 3), the combined organic phase washed with brine and dried by Na_2SO_4, filtered, concentrated under reduced pressure to afford the crude product and the crude product recrystallization from ethyl acetate and petroleum ether. The yellow needles solid **1** was obtained.

4. General procedure for the preparation of substrates 2.[4]



m-Chloroperbenzoic acid (70%, 14.4 g, 62.5 mmol, 2.5 equiv.) was added portion-wise to a solution of benzo[*b*]thiophene (R^2 = H) (3.36 g, 25 mmol) in chloroform (100 mL) at room temperature with vigorous stirring. The mixture was allowed to stir overnight at the same temperature. Then, a saturated aqueous $NaHCO_3$ solution was added and the aqueous layer was extracted with dichloromethane (50 mL × 3). The collected organic layers were dried, and the solvent was removed in vacuo. Crystallization **2** (R = H) from ethanol afforded white crystals (3g, 72% yield).

References

[1] X. Yang, Y.-H. Zhou, H. Yang, S.-S. Wang, Q. Ouyang, Q.-L. Luo and Q.-X. Guo, *Org. Lett.*, **2019**, *21*, 1161.

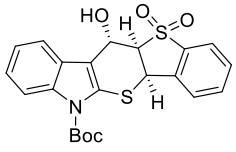
[2] H.-B. Deng and J. P. Konopelski, *Org. Lett.*, **2001**, *19*, 3001.

[3] L.-L. Wu, Y.-M. Wang and Z.-H. Zhou, *Tetrahedron: Asymmetry*, **2014**, *25*, 1389.

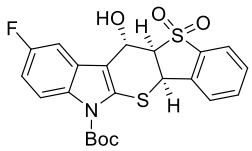
[4] D. Madec, F. Mingoia and G. Poli, *Eur. J. Org. Chem*. **2005**, 552.

5. General procedure for the asymmetric reaction of compounds 3.

To a reaction tube were added the 2-mercaptoindole-3-carbaldehydes **1** (0.11 mmol, 1.1 equiv.), benzo[*b*]thiophene 1,1-dioxide **1** (0.1 mmol, 1.0 equiv.), catalyst **D** (0.01 mmol) and toluene (0.5 mL). The reaction mixture was stirred at 0 °C for 48 h. the reaction mixture was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 4:1～3:1) to afford the desired product **3**.

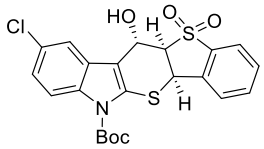


***tert*-butyl(6a*R*,11a*R*,12*S*)-12-hydroxy-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-b]indole-5(6a*H*)-carboxylate 11,11-dioxide (3a)** : white solid; 99% yield; 98% ee; >20:1 dr, $[\alpha]_D^{20}$ = +75.2 (*c* 1.0, CH_2Cl_2); m.p.183.4-185.1 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (70/30 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 11.98 min, t_{minor} = 7.72 min); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.00-7.92 (m, 1H), 7.89 (d, *J* = 7.6 Hz, 1H), 7.77 (t, *J* = 4.5 Hz, 3H), 7.67 (m, *J* = 8.2, 1H), 7.32-7.23 (m, 2H), 6.41 (d, *J* = 7.1 Hz, 1H), 5.42 (dd, *J* = 7.2, 3.0 Hz, 1H), 5.34 (d, *J* = 6.6 Hz, 1H), 4.41 (dd, *J* = 6.6, 3.0 Hz, 1H), 1.62 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 149.6, 137.6, 137.4, 135.0, 134.4, 130.7, 128.9, 128.2, 127.0, 123.7, 123.2, 122.2, 118.6, 114.6, 85.7, 79.2, 67.3, 58.3, 27.7. HRMS (ESI) Calcd. for $C_{22}H_{21}NNaO_5S_2$ $[M + H]^+$ 466.0753; found: 466.0768.

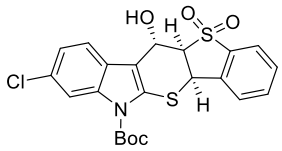


***tert*-butyl(6a*R*,11a*R*,12*S*)-2-fluoro-12-hydroxy-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-*b*]indole-5(6a*H*)-carboxylate 11,11-dioxide (3b):** white solid; 99% yield; 97% ee; 10:1 dr, $[\alpha]_D^{20}$ = +51.4 (*c* 1.0, CH_2Cl_2); m.p.313.2.-314.4 ℃; The ee was

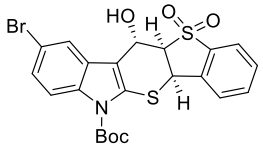
determined by HPLC analysis using a Chiralpak OD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 9.98 min, t_{minor} = 5.67 min) ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.98-7.87 (m, 2H), 7.84-7.75 (m, 2H), 7.68 (m, 1H), 7.53 (dd, *J* = 9.2, 2.7 Hz, 1H), 7.11 (td, *J* = 9.2, 2.7 Hz, 1H), 6.40 (d, *J* = 7.1 Hz, 1H), 5.44-5.32 (m, 2H), 4.42 (dd, *J* = 6.6, 3.1 Hz, 1H), 1.62 (s, 9H). ^{13}C NMR (75 MHz, DMSO-d_6) δ, 158.7 (d, *J* = 237.5 Hz) 149.2, 137.5, 137.2, 134.4, 131.4, 130.6, 130.2, 129.9 (d, *J* = 10.4 Hz), 126.9, 122.2, 115.8 (d, *J* = 9.3 Hz), 114.3 (d, *J* = 3.7 Hz), 110.9 (d, *J* = 25.0 Hz), 104.2 (d, *J* = 24.6 Hz), 85.9, 66.9, 58.0, 54.9, 27.6; HRMS (ESI) Calcd. for $C_{22}H_{20}FNNaO_5S_2$ [M+Na]$^+$: 484.0659; found: 484.0647.



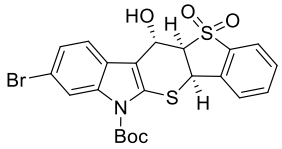
***tert*-butyl(6a*R*,11a*R*,12*S*)-2-chloro-12-hydroxy-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-*b*]indole-5(6a*H*)-carboxylate 11,11-dioxide (3c):** white solid; 98% yield; 95% ee; 7:1 dr, $[\alpha]_D^{20}$ = +95.2 (*c* 1.0, CH_2Cl_2); m.p.159.6-160.3 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 10.84 min, t_{minor} = 5.68 min) ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.92 (t, *J* = 7.6 Hz, 2H), 7.84-7.75 (m, 3H), 7.68 (m, 1H), 7.30 (dd, *J* = 8.8, 2.2 Hz, 1H), 6.43 (d, *J* = 7.0 Hz, 1H), 5.41 (dd, *J* = 7.0, 3.1 Hz, 1H), 5.35 (d, *J* = 6.7 Hz, 1H), 4.43 (dd, *J* = 6.6, 3.1 Hz, 1H), 1.62 (s, 9H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 149.1, 137.5, 137.1, 134.3, 133.4, 130.6, 130.1, 128.0, 127.7, 126.9, 123.3, 122.1, 117.9, 115.9, 114.0, 86.1, 79.2, 67.0, 58.1, 27.6; HRMS (ESI) Calcd. for $C_{22}H_{20}ClNNaO_5S_2$ [M+Na]$^+$: 500.0364; found: 500.0346.



***tert*-butyl(6a*R*,11a*R*,12*S*)-3-chloro-12-hydroxy-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-b]indole-5(6a*H*)-carboxylate 11,11-dioxide (3d):** white solid; 96% yield; 97% ee; >20:1 dr, $[\alpha]_D^{20}$ = +88.4 (*c* 1.0, CH_2Cl_2); m.p.292.3-293.5 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 10.45 min, t_{minor} = 7.08 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.97 (d, *J* = 1.9 Hz, 1H), 7.91 (d, *J* = 7.6 Hz, 1H), 7.84-7.74 (m, 3H), 7.68 (m, 1H), 7.34 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.45 (d, *J* = 7.2 Hz, 1H), 5.40 (dd, *J* = 7.2, 3.2 Hz, 1H), 5.35 (d, *J* = 6.7 Hz, 1H), 4.42 (dd, *J* = 6.7, 3.2 Hz, 1H), 1.62 (s, 9H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 149.0, 137.6, 137.0, 135.3, 134.4, 130.7, 129.1, 128.1, 127.6, 127.0, 123.4, 122.2, 119.8, 114.7, 114.4, 86.3, 67.2, 58.4, 54.9, 27.6; HRMS (ESI) Calcd. for $C_{22}H_{20}ClNNaO_5S_2$ [M+Na]$^+$: 500.0364; found: 500.0349.



***tert*-butyl(6a*R*,11a*R*,12*S*)-2-bromo-12-hydroxy-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-*b*]indole-5(6a*H*)-carboxylate 11,11-dioxide (3e):** white solid; 95% yield; 93% ee; >20:1 dr, $[\alpha]_D^{20}$ = +90.4 (*c* 1.0, CH_2Cl_2); m.p.186.1.-187.3 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 8.62 min, t_{minor} = 5.32 min) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, *J* = 2.0 Hz, 1H), 7.82 (d, *J* = 8.3 Hz, 2H), 7.67 (dt, *J* = 14.6, 7.6 Hz, 2H), 7.55 (t, *J* = 7.3 Hz, 1H), 7.32-7.26 (m, 1H), 5.22 (dd, *J* = 7.1, 4.4 Hz, 1H), 5.13 (d, *J* = 5.8 Hz, 1H), 3.90 (t, *J* = 6.4 Hz, 1H), 3.64 (d, *J* = 4.5 Hz, 1H), 1.72 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 138.6, 136.8, 134.4, 130.4, 130.3, 128.7, 126.5, 126.2, 122.8, 122.3, 116.9, 116.2, 112.0, 86.6, 67.3, 62.6, 40.4, 28.4; HRMS (ESI) Calcd. for $C_{22}H_{20}BrNNaO_5S_2$ [M+Na]$^+$: 543.9858; found: 543.9839.



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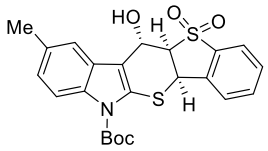
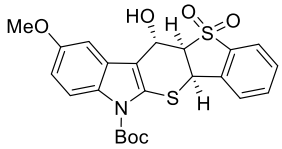
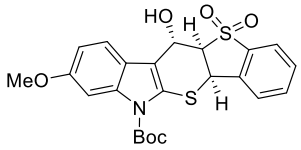


***tert*-butyl(6a*R*,11a*R*,12*S*)-12-hydroxy-2-methyl-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-*b*]indole-5(6a*H*)-carboxylate 11,11-dioxide(3g):** white solid; 98% yield; 93% ee; >20:1 dr, $[\alpha]_D^{20}$ = +75.4 (*c* 1.0, CH_2Cl_2); m.p.184.5.-185.3 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 9.89 min, t_{minor} = 6.08 min);^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 10.6, 8.0 Hz, 2H), 7.69 (d, *J* = 7.7 Hz, 1H), 7.62 (td, *J* = 7.5, 1.3 Hz, 1H), 7.54 (d, *J* = 7.3 Hz, 2H), 7.05 (s, 1H), 5.30 (d, *J* = 6.5 Hz, 1H), 5.07 (d, *J* = 5.8 Hz, 1H), 3.88 (t, *J* = 6.2 Hz, 1H), 3.50 (s, 1H), 2.39 (s, 3H), 1.72 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.4, 138.7, 137.1, 134.3, 133.8, 133.1, 130.2, 128.9, 127.2, 126.1, 125.1, 122.7, 119.4, 114.6, 112.5, 85.8, 67.5, 62.4, 40.4, 28.4, 21.4; HRMS (ESI) Calcd. for $C_{23}H_{23}NNaO_5S_2$ $[M+Na]^+$: 480.0910; found: 480.0901.

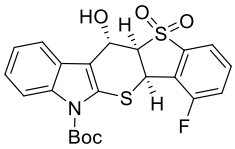


***tert*-butyl(6a*R*,11a*R*,12*S*)-12-hydroxy-2-methoxy-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-*b*]indole-5(6a*H*)-carboxylate 11,11-dioxide (3h):** white solid; 96% yield; 97% ee; >20:1 dr, $[\alpha]_D^{20}$ = +94.8 (*c* 1.0, CH_2Cl_2); m.p.193.2.-194.7 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 9.99 min, t_{minor} = 7.17 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (t, *J* = 8.4 Hz, 2H), 7.70 (d, *J* = 7.7 Hz, 1H), 7.63 (td, *J* = 7.4, 1.2 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.24 (d, *J* = 2.6 Hz, 1H), 6.81 (dd, *J* = 9.1, 2.7 Hz, 1H), 5.28 (dd, *J* = 6.8, 4.3 Hz, 1H), 5.10 (d, *J* = 5.8 Hz, 1H), 3.91 (t, *J* = 6.3 Hz, 1H), 3.81 (s, 3H), 3.53 (d, *J* = 4.8 Hz, 1H), 1.71 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.3, 150.3, 138.8, 137.0, 134.3, 130.2, 129.6, 127.7, 126.2, 122.7, 115.7, 112.5, 102.1, 85.8, 67.5, 62.6, 55.8, 40.4, 28.4; HRMS (ESI) Calcd. for $C_{23}H_{23}NNaO_6S_2$ $[M+Na]^+$: 496.0859; found: 496.0855.

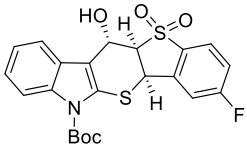


***tert*-butyl(6aR,11a*R*,12*S*)-12-hydroxy-3-methoxy-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-*b*]indole-5(6a*H*)-carboxylate 11,11-dioxide (3i):** white solid; 98% yield; 99% ee; >20:1 dr, $[\alpha]_D^{20}$ = +29.4 (*c* 1.0, CH_2Cl_2); m.p.188.6-189.3 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 9.76 min, t_{minor} = 7.24 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.79 (d, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 7.7 Hz, 1H), 7.67-7.57 (m, 3H), 7.52 (d, *J* = 7.4 Hz, 1H), 6.84 (d, *J* = 2.1 Hz, 1H), 5.26 (dd, *J* = 7.0, 3.6 Hz, 1H), 5.06 (d, *J* = 5.9 Hz, 1H), 3.89 (s, 1H), 3.82 (s, 3H), 3.57 (d, *J* = 4.7 Hz, 1H), 1.72 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.3, 150.3, 138.7,

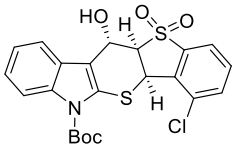
137.1, 136.7, 134.3, 130.2, 126.2, 124.9, 122.6, 120.1, 113.2, 111.9, 100.1, 85.8, 67.7, 62.9, 55.7, 40.7, 28.4; HRMS (ESI) Calcd. for $C_{23}H_{23}NNaO_6S_2$ $[M+Na]^+$: 496.0859; found: 496.0861.



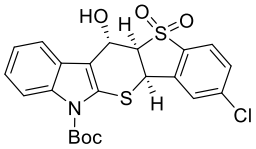
***tert*-butyl(6a*R*,11a*R*,12*S*)-7-fluoro-12-hydroxy-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-*b*]indole-5(6a*H*)-carboxylate 11,11-dioxide (3j):** white solid; 99% yield; 99% ee; >20:1 dr, $[\alpha]_D^{20}$ = +0.5 (*c* 1.0, CH_2Cl_2); m.p.313..2-314.4 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 5.33 min, t_{minor} = 4.76 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03-7.95 (m, 1H), 7.75-7.66 (m, 1H), 7.64 -7.53 (m, 2H), 7.36 (m, 1H), 7.29-7.20 (m, 3H), 5.67 (s, 1H), 5.25 (d, *J* = 6.8 Hz, 1H), 4.17 (dd, *J* = 6.8, 3.0 Hz, 1H), 2.96 (d, *J* = 5.2 Hz, 1H), 1.67 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1 (d, *J* = 256.8 Hz), 150.2, 140.1, 135.9, 132.8 (d, *J* = 7.0 Hz), 128.9, 128.6, 124.4 (d, *J* = 20.3 Hz), 124.1, 123.6, 121.0 (d, *J* = 20.0 Hz), 118.5 (d, *J* = 4.3 Hz), 118.0, 115.2, 112.7, 86.1, 67.2, 59.9, 35.1, 28.3; HRMS (ESI) Calcd. for $C_{22}H_{20}FNNaO_5S_2$ $[M+Na]^+$: 484.0659; found: 484.0650.



***tert*-butyl(6a*R*,11a*R*,12*S*)-8-fluoro-12-hydroxy-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-*b*]indole-5(6a*H*)-carboxylate 11,11-dioxide (3k):** white solid; 97% yield; 98% ee; 13:1 dr, $[\alpha]_D^{20}$ = +82.1 (*c* 1.0, CH_2Cl_2); m.p.180.3-181.2 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (70/30 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 13.17 min, t_{minor} = 9.68 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06-7.89 (m, 1H), 7.76 (2H), 7.40 (d, J = 8.1 Hz, 1H), 7.30-7.11 (m, 3H), 5.30 (d, J = 3.4 Hz, 1H), 5.03 (d, J = 5.8 Hz, 1H), 3.88 (t, J = 6.3 Hz, 1H), 3.56 (d, J = 4.9 Hz, 1H), 1.74 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2 (d, *J* = 257.0 Hz), 150.4, 142.5 (d, *J* = 9.1 Hz), 135.6, 132.9, 128.7, 126.8, 125.2 (d, *J* = 9.9 Hz), 124.0, 123.5, 119.6, 117.9 (d, *J* = 24.0 Hz), 114.9, 113.7 (d, *J* = 24.7 Hz), 112.6, 86.2, 67.7, 62.5, 40.1, 28.4; HRMS (ESI) Calcd. for $C_{22}H_{20}FNNaO_5S_2$ $[M+Na]^+$: 484.0659 found: 484.0649.

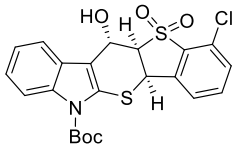


***tert*-butyl(6a*R*,11a*R*,12*S*)-7-chloro-12-hydroxy-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-*b*]indole-5(6a*H*)-carboxylate 11,11-dioxide (3l):** white solid; 98% yield; 97% ee; >20:1 dr, $[\alpha]_D^{20}$ = +0.4 (*c* 1.0, CH_2Cl_2); m.p.195.4-196.3 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 5.32 min, t_{minor} = 4.70 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04-7.94 (m, 1H), 7.73-7.59 (m, 3H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.26-7.19 (m, 2H), 5.73 (s, 1H), 5.28 (d, *J* = 6.6 Hz, 1H), 4.21 (dd, *J* = 6.7, 2.1 Hz, 1H), 2.93 (s, 1H), 1.66 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.2, 139.6, 135.8, 135.3, 134.3, 133.1, 131.8, 129.3, 128.7, 124.0, 123.6, 121.1, 117.4, 115.2, 111.8, 86.0, 66.6, 58.5, 37.0, 28.3; HRMS (ESI) Calcd. for $C_{22}H_{20}ClNNaO_5S_2$ $[M+Na]^+$: 500.0364; found; 500.0368.

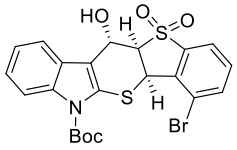


***tert*-butyl(6a*R*,11a*R*,12*S*)-8-chloro-12-hydroxy-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-*b*]indole-5(6a*H*)-carboxylate 11,11-dioxide (3m)：** white solid; 98% yield; 98% ee; 13:1 dr, $[\alpha]_D^{20}$ = +145.3 (*c* 1.0, CH_2Cl_2); m.p.127.3-128.2 ℃; The ee was determined by HPLC analysis using a Chiralpak IC-H column (30/70 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 10.13 min, t_{minor} = 8.36 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01-7.91 (m, 1H), 7.78-7.65 (m, 3H), 7.49 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.25-7.16 (m, 2H), 5.28 (t, *J* = 5.4 Hz, 1H), 5.01 (d, *J* = 5.7 Hz, 1H), 3.86 (t, *J* = 6.2 Hz, 1H), 3.58 (d, *J* = 4.6 Hz, 1H), 1.74 (s, 9H).

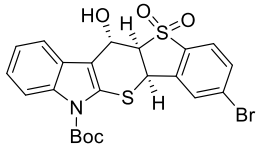
^{13}C NMR (100 MHz, $CDCl_3$) δ 150.4, 141.0, 140.9, 135.6, 135.5, 130.6, 128.7, 126.9, 126.5, 124.0, 124.0, 123.5, 119.5, 114.9, 112.6, 86.2, 67.5, 62.3, 40.0, 28.4; HRMS (ESI) Calcd. for $C_{22}H_{20}ClNNaO_5S_2$ [M+Na]$^+$: 500.0364; found: 500.0348.



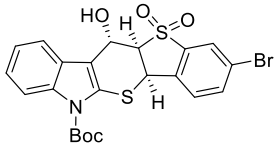
***tert*-butyl(6a*R*,11a*R*,12*S*)-12-hydroxy-10-chloro-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-*b*]indole-5(6a*H*)-carboxylate 11,11-dioxide (3n):** white solid; 99% yield; 78% ee; >20:1 dr, $[\alpha]_D^{20}$ = +10.3 (*c* 1.0, CH_2Cl_2); m.p.303.1-304.3 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 8.96 min, t_{minor} = 6.31 min) ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.96 (dd, *J* = 6.2, 3.3 Hz, 1H), 7.84-7.66 (m, 4H), 7.28 (dd, *J* = 6.0, 3.2 Hz, 2H), 6.43 (s, 1H), 5.43 (s, 1H), 5.34 (d, *J* = 6.7 Hz, 1H), 4.55 (dd, *J* = 6.8, 2.8 Hz, 1H), 1.62 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 149.4, 140.4, 135.8, 134.9, 134.5, 131.3, 128.8, 128.2, 127.8, 125.8, 123.7, 123.1, 118.5, 114.5, 114.3, 85.6, 67.6, 58.0, 38.3, 27.6; HRMS (ESI) Calcd. for $C_{22}H_{20}ClNNaO_5S_2$ [M+Na]$^+$: 500.0364; found: 500.0357.



***tert*-butyl(6a*R*,11a*R*,12*S*)-7-bromo-12-hydroxy-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-b]indole-5(6a*H*)-carboxylate 11,11-dioxide (3o):** white solid; 99% yield; 97% ee; >20:1 dr, $[\alpha]_D^{20}$ = +276.9 (*c* 1.0, CH_2Cl_2); m.p.194.4-195.3 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 5.64 min, t_{minor} = 4.96 min) ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.06 (d, *J* = 7.9 Hz, 1H), 8.00-7.89 (m, 2H), 7.77-7.68 (m, 1H), 7.63 (t, *J* = 7.8 Hz, 1H), 7.36-7.23 (m, 2H), 6.27 (d, *J* = 7.6 Hz, 1H), 5.47 (dd, *J* = 7.6, 1.9 Hz, 1H), 5.33 (d, *J* = 6.6 Hz, 1H), 4.69 (dd, *J* = 6.6, 2.0 Hz, 1H), 1.62 (s, 9H). ^{13}C NMR (101 MHz, DMSO) δ 149.5, 139.2, 137.6, 137.4, 134.9, 132.5, 128.9, 127.9, 123.6, 123.2, 121.5, 121.5, 117.9, 114.6, 112.9, 85.7, 65.5, 56.3, 38.8, 27.7; HRMS (ESI) Calcd. for $C_{22}H_{20}BrNNaO_5S_2$ [M+Na]$^+$: 543.9858; found: 543.9840.

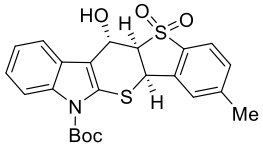


***tert*-butyl(6a*R*,11a*R*,12*S*)-8-bromo-12-hydroxy-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-*b*]indole-5(6a*H*)-carboxylate 11,11-dioxide (3p):** white solid; 99% yield; 98% ee; 12:1 dr, $[\alpha]_D^{20}$ = +165.5 (*c* 1.0, CH_2Cl_2); m.p.137.1-138.2 ℃; The ee was determined by HPLC analysis using a Chiralpak IC-H column (30/70 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 9.65 min, t_{minor} = 8.14 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01-7.92 (m, 1H), 7.86-7.82 (m, 1H), 7.78-7.70 (m, 1H), 7.68-7.62 (m, 2H), 7.25-7.18 (m, 2H), 5.28 (dd, *J* = 6.9, 4.1 Hz, 1H), 5.02 (d, *J* = 5.7 Hz, 1H), 3.85 (t, *J* = 6.3 Hz, 1H), 3.56 (d, *J* = 4.7 Hz, 1H), 1.74 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.4, 141.0, 136.0, 135.6, 133.5, 129.5, 129.3, 128.7, 126.9, 124.1, 124.0, 123.5, 119.5, 114.9, 112.6, 86.2, 67.5, 62.3, 40.0, 28.4; HRMS (ESI) Calcd. for $C_{22}H_{20}BrNNaO_5S_2$ [M+Na]$^+$: 543.9858; found: 543.9841.

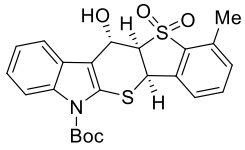


***tert*-butyl(6a*R*,11a*R*,12*S*)-7-bromo-12-hydroxy-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-b]indole-5(6a*H*)-carboxylate 11,11-dioxide (3q):** white solid; 99% yield; 99% ee; >20:1 dr, $[\alpha]_D^{20}$ = +85.4 (*c* 1.0, CH_2Cl_2); m.p.184.3-185.6 ℃; The ee was determined by HPLC analysis using a Chiralpak IC-H column (30/70 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 8.29 min, t_{minor} = 7.17 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.18 (d, *J* = 1.8 Hz, 1H), 7.96 (m, 2H), 7.74 (dd, *J* = 6.9, 3.2 Hz, 2H), 7.33-7.23 (m, 2H), 6.40 (d, *J* = 7.1 Hz, 1H), 5.40 (dd, *J* = 7.1, 3.0 Hz, 1H), 5.31 (d, *J* = 6.5 Hz, 1H), 4.48 (dd, *J* = 6.6, 2.9 Hz, 1H), 1.62

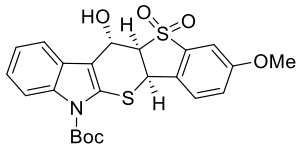
(s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 149.5, 139.5, 137.3, 136.9, 135.0, 129.1, 128.8, 128.0, 125.1, 123.8, 123.3, 123.2, 118.5, 114.6, 114.4, 85.8, 67.5, 58.1, 38.7, 27.7; HRMS (ESI) Calcd. for $C_{22}H_{20}BrNNaO_5S_2$ [M+Na]$^+$: 543.9858; found: 543.9838.



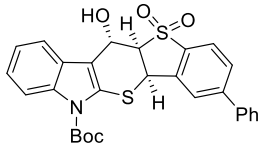
***tert*-butyl(6aR,11a*R*,12*S*)-12-hydroxy-8-methyl-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-b]indole-5(6a*H*)-carboxylate 11,11-dioxide (3r):** white solid; 98% yield; 98% ee; >20:1 dr, $[\alpha]_D^{20}$ = +87.4 (*c* 1.0, CH_2Cl_2); m.p.185.3-185.8 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 12.73 min, t_{minor} = 10.03 min); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.94 (dd, *J* = 6.4, 3.0 Hz, 1H), 7.76 (dd, *J* = 8.5, 3.7 Hz, 2H), 7.56 (s, 1H), 7.47 (d, *J* = 7.9 Hz, 1H), 7.31-7.24 (m, 2H), 6.37 (dd, *J* = 7.1, 2.3 Hz, 1H), 5.38 (m, 1H), 5.27 (d, *J* = 6.6 Hz, 1H), 4.36 (dd, *J* = 6.6, 3.0 Hz, 1H), 2.44 (s, 3H), 1.62 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 149.6, 145.2, 137.6, 134.9, 134.9, 131.3, 128.9, 128.2, 127.1, 123.7, 123.2, 122.0, 118.6, 114.6, 85.7, 67.4, 58.3, 39.0, 27.7, 21.3; HRMS (ESI) Calcd. for $C_{23}H_{23}NNaO_5S_2$ [M+Na]$^+$: 480.0910; found: 480.0904.



***tert*-butyl(6a*R*,11a*R*,12*S*)-12-hydroxy-10-methyl-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-*b*]indole-5(6a*H*)-carboxylate 11,11-dioxide (3s):** white solid; 81% yield; 61% ee; >20:1 dr, $[\alpha]_D^{20}$ = +13.2 (*c* 1.0, CH_2Cl_2); m.p.191.8.-192.4 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 7.29 min, t_{minor} = 5.46 min) ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.99-7.93 (m, 1H), 7.80-7.74 (m, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 7.28 (dd, *J* = 6.0, 3.2 Hz, 2H), 6.38 (d, *J* = 7.2 Hz, 1H), 5.40 (dd, *J* = 7.2, 3.0 Hz, 1H), 5.29 (d, *J* = 6.8 Hz, 1H), 4.39 (dd, *J* = 6.8, 3.0 Hz, 1H), 2.53 (s, 3H), 1.62 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 149.5, 137.5, 135.5, 135.0, 134.9, 134.1, 132.1, 128.9, 128.1, 124.3, 123.7, 123.2, 118.5, 114.6, 114.5, 85.6, 67.3, 58.3, 38.8, 27.7, 16.4; HRMS (ESI) Calcd. for $C_{23}H_{23}NNaO_5S_2$ [M+Na]$^+$: 480.0910; found: 480.0913.

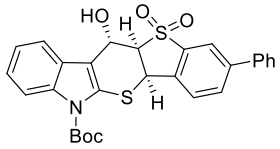


***tert*-butyl(6a*R*,11a*R*,12*S*)-12-hydroxy-9-methoxy-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-*b*]indole-5(6a*H*)-carboxylate 11,11-dioxide (3t):** white solid; 99% yield; 99% ee; >20:1 dr, $[\alpha]_D^{20}$ = +113.3 (*c* 1.0, CH_2Cl_2); m.p.182.3-183.8 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 13.43 min, t_{minor} = 10.44 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.01-7.93 (m, 1H), 7.82-7.73 (m, 1H), 7.68 (d, *J* = 8.6 Hz, 1H), 7.43 (d, *J* = 2.5 Hz, 1H), 7.36-7.23 (m, 3H), 6.37 (d, *J* = 7.2 Hz, 1H), 5.40 (dd, *J* = 7.1, 3.1 Hz, 1H), 5.25 (d, *J* = 6.7 Hz, 1H), 4.39 (dd, *J* = 6.7, 3.1 Hz, 1H), 3.87 (s, 3H), 1.62 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 160.8, 149.4, 139.0, 135.0, 128.8, 128.7, 128.2, 128.1, 123.6, 123.1, 121.6, 118.6, 114.9, 114.5, 105.6, 85.5, 68.3, 58.7, 56.2, 38.8, 27.7; HRMS (ESI) Calcd. for $C_{23}H_{23}NNaO_6S_2$ [M+Na]$^+$: 496.0859; found: 496.0845.



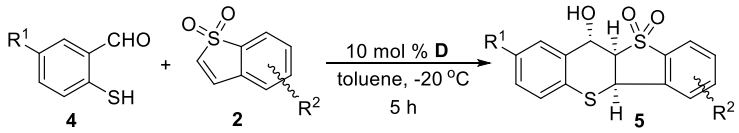
***tert*-butyl(6a*R*,11a*R*,12*S*)-12-hydroxy-8-phenyl-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-*b*]indole-5(6a*H*)-carboxylate 11,11-dioxide (3u):** white solid; 98% yield; 98% ee; >20:1 dr, $[\alpha]_D^{20}$ = +208.4 (*c* 1.0, CH_2Cl_2); m.p.182.3-183.7 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 8.44 min, t_{minor} = 6.94 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01-

7.93 (m, 1H), 7.86 (d, *J* = 7.8 Hz, 2H), 7.82-7.70 (m, 2H), 7.62-7.53 (m, 2H), 7.47 (q, *J* = 8.3, 7.3 Hz, 3H), 7.21 (dd, *J* = 5.8, 2.9 Hz, 2H), 5.36 (dd, *J* = 6.8, 4.5 Hz, 1H), 5.15 (d, *J* = 5.8 Hz, 1H), 3.94 (t, *J* = 6.2 Hz, 1H), 3.60 (d, *J* = 4.7 Hz, 1H), 1.73 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.5, 147.8, 139.5, 139.1, 135.6, 135.5, 129.2, 129.2, 129.0, 128.8, 127.6, 124.7, 123.8, 123.5, 123.1, 119.6, 114.9, 112.8, 86.0, 67.7, 62.6, 40.4, 28.4; HRMS (ESI) Calcd. for $C_{28}H_{25}NNaO_5S_2$ [M+Na]$^+$: 542.1066; found: 542.1056.

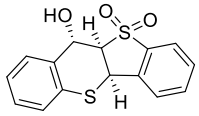


***tert*-butyl(6a*R*,11a*R*,12*S*)-12-hydroxy-9-phenyl-11a,12-dihydrobenzo[4',5']thieno[2',3':5,6]thiopyrano[2,3-*b*]indole-5(6a*H*)-carboxylate 11,11-dioxide (3v):** white solid; 98% yield; 99% ee; >20:1 dr, $[\alpha]_D^{20}$ = +98.2 (*c* 1.0, CH_2Cl_2); m.p.106.5-107.5 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 8.44 min, t_{minor} = 6.73 min) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (q, *J* = 3.8 Hz, 2H), 7.86-7.71 (m, 3H), 7.56 (dt, *J* = 5.8, 1.7 Hz, 2H), 7.51-7.37 (m, 3H), 7.25-7.15 (m, 2H), 5.39 (d, *J* = 6.5 Hz, 1H), 5.13 (d, *J* = 5.9 Hz, 1H), 3.96 (t, *J* = 6.2 Hz, 1H), 3.57 (s, 1H), 1.74 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.4, 143.9, 138.7, 137.8, 137.3, 135.7, 133.1, 129.3, 128.8, 128.7, 127.3, 126.5, 123.9, 123.5, 121.0, 119.5, 114.9, 112.9, 86.0, 67.8, 62.5, 40.2, 28.4; HRMS (ESI) Calcd. for $C_{28}H_{25}NNaO_5S_2$ [M+Na]$^+$: 542.1066; found: 542.1067.

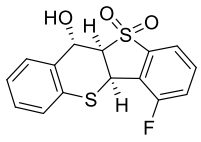
6. General experimental procedures for asymmetric synthesis of compounds 5



To a reaction tube were added, the benzo[*b*]thiophene 1,1-dioxide **2** (0.1 mmol, 1.0 equiv.), 2-mercaptobenzaldehyde **4** (0.11 mmol, 1.1 equiv.), catalyst **D** (0.01 mmol) and toluene (0.5 mL). The reaction mixture was stirred at -20 ºC, and monitored by TLC. the reaction mixture was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford the desired product **5.**

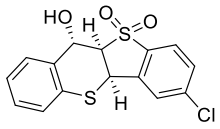


(5aR,10aR,11S)-11-hydroxy-5a,10a-dihydro-11H-benzo[4,5]thieno[3,2-b]thiochromene 10,10-dioxide (5a) : white solid; 92% yield; 93% ee; >20:1 dr, $[\alpha]_D^{20}$ = +158.3 (*c* 1.0, CH_2Cl_2); m.p.260.1-261.7 ℃; The ee was determined by HPLC analysis using a Chiralpak AD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 10.02 min, t_{minor} = 9.25 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.92 (d, *J* = 7.3 Hz, 1H), 7.84-7.75 (m, 1H), 7.71 (t, *J* = 6.6 Hz, 3H), 7.56-7.49 (m, 1H), 7.48-7.39 (m, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 6.62 (d, *J* = 6.5 Hz, 1H), 5.17-5.07 (m, 1H), 5.05 (d, *J* = 8.6 Hz, 1H), 4.00 (t, *J* = 8.9 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 141.6, 140.0, 134.4, 134.3, 131.9, 130.8, 129.2, 127.9, 127.6, 127.4, 125.0, 121.5, 68.8, 68.0, 44.4; HRMS (ESI) Calcd. for $C_{15}H_{12}NaO_3S_2$ [M+Na]$^+$: 327.0120; found: 327.0132.

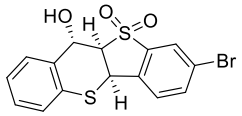


(5a*R*,10a*R*,11*S*)-6-fluoro-11-hydroxy-5a,10a-dihydro-11*H*-benzo[4,5]thieno[3,2-*b*]thiochromene 10,10-dioxide (5b): white solid; 98% yield; 95% ee; >20:1 dr, $[\alpha]_D^{20}$ = +222.3 (*c* 1.0, CH_2Cl_2); m.p.178.4-179.7 ℃; The ee was determined by HPLC analysis using a Chiralpak AD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 11.63 min, t_{minor} = 7.11 min); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.6 Hz, 1H), 7.64 (m, 2H), 7.56-7.47 (m, 1H), 7.46-7.29 (m, 3H), 5.43 (dd, *J* = 9.0, 4.3 Hz, 1H), 4.93 (d, *J* = 8.9 Hz, 1H), 3.83 (t, *J* = 9.0 Hz, 1H), 3.70 (d, *J* =

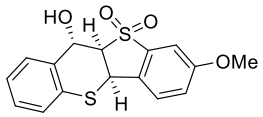
5.3 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ159.8 (d, *J* = 258.0 Hz), 141.9 (d, *J* = 3.1 Hz), 139.6, 133.2 (d, *J* = 7.1 Hz), 131.7, 129.8, 128.2, 128.0, 124.9, 122.4 (d, *J* = 19.8 Hz), 121.0 (d, *J* = 19.9 Hz), 118.0 (d, *J* = 4.3 Hz), 70.1, 69.5, 40.9; HRMS (ESI) Calcd. for $C_{15}H_{11}FNaO_3S_2$ $[M+Na]^+$: 345.0026; found: 345.0035.



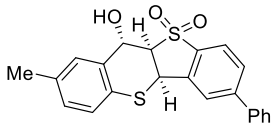
(5a*R*,10a*R*,11*S*)-7-chloro-11-hydroxy-5a,10a-dihydro-11*H*-benzo[4,5]thieno[3,2-*b*]thiochromene 10,10-dioxide (5c): white solid; 98% yield; 93% ee; >20:1 dr, $[\alpha]_D^{20}$ = +101.3 (*c* 1.0, CH_2Cl_2); m.p.221.4-222.7 ℃; The ee was determined by HPLC analysis using a Chiralpak AD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 19.01 min, t_{minor} = 11.74 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.97 (d, *J* = 8.3 Hz, 1H), 7.81 (d, *J* = 1.9 Hz, 1H), 7.78-7.66 (m, 2H), 7.50 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.44 (td, *J* = 7.5, 1.5 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 6.67 (d, *J* = 6.5 Hz, 1H), 5.10 (dd, *J* = 9.1, 5.8 Hz, 1H), 5.01 (d, *J* = 8.6 Hz, 1H), 4.05 (t, *J* = 8.9 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 141.5, 139.1, 138.9, 136.9, 131.7, 131.3, 129.3, 127.9, 127.8, 127.6, 125.2, 123.5, 69.3, 68.1, 44.0; HRMS (ESI) Calcd. for $C_{15}H_{11}lNaO_3S_2$ $[M+Na]^+$: 360.9370; found: 360.9373.



(5a*R*,10a*R*,11*S*)-8-bromo-11-hydroxy-5a,10a-dihydro-11*H*-benzo[4,5]thieno[3,2-*b*]thiochromene 10,10-dioxide (5d): white solid; 90% yield; 96% ee; >20:1 dr, $[\alpha]_D^{20}$ = +158.5 (*c* 1.0, CH_2Cl_2); m.p.240.1-241.7 ℃; The ee was determined by HPLC analysis using a Chiralpak AD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 18.92 min, t_{minor} = 11.72 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.23 (d, *J* = 1.9 Hz, 1H), 7.97 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.68 (dd, *J* = 14.6, 7.9 Hz, 2H), 7.51 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.44 (td, *J* = 7.5, 1.4 Hz, 1H), 7.34 (t, *J* = 7.4 Hz, 1H), 6.66 (d, *J* = 6.5 Hz, 1H), 5.10 (t, *J* = 7.8 Hz, 1H), 5.01 (d, *J* = 8.6 Hz, 1H), 4.05 (t, *J* = 8.9 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 141.9, 141.4, 137.3, 133.7, 131.7, 130.0, 129.2, 127.7, 127.5, 125.1, 124.3, 123.5, 69.4, 68.0, 44.0; HRMS (ESI) Calcd. for $C_{15}H_{11}BrNaO_3S_2$ $[M+Na]^+$: 404.9225; found: 404.9213.



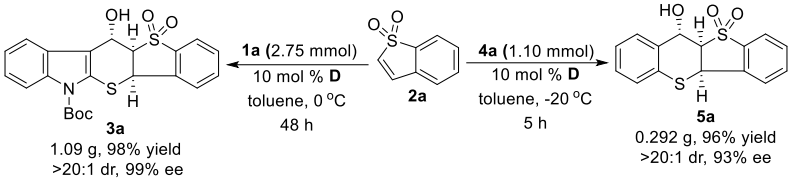
(5a*R*,10a*R*,11*S*)-11-hydroxy-8-methoxy-5a,10a-dihydro-11H-benzo[4,5]thieno[3,2-*b*]thiochromene 10,10-dioxide (5e): white solid; 99% yield; 96% ee; >20:1 dr, $[\alpha]_D^{20}$ = +166.8 (*c* 1.0, CH_2Cl_2); m.p.224.5-225.1 ℃; The ee was determined by HPLC analysis using a Chiralpak AD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 17.73 min, t_{minor} = 12.66 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.71 (d, *J* = 7.6 Hz, 1H), 7.58 (d, *J* = 8.6 Hz, 1H), 7.55-7.38 (m, 3H), 7.33 (dt, *J* = 8.7, 2.6 Hz, 2H), 6.59 (d, *J* = 4.7 Hz, 1H), 5.11 (t, *J* = 7.7 Hz, 1H), 4.94 (d, *J* = 8.6 Hz, 1H), 4.01 (t, *J* = 8.8 Hz, 1H), 3.88 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 161.0, 141.6, 141.3, 132.0, 129.2, 128.9, 127.5, 127.4, 126.1, 125.0, 122.3, 104.3, 69.8, 68.2, 56.2, 44.0; HRMS (ESI) Calcd. for $C_{16}H_{14}NaO_4S_2$ $[M+Na]^+$: 357.0226; found: 357.0231.



(5a*R*,10a*R*,11*S*)-11-hydroxy-2-methyl-7-phenyl-5a,10a-dihydro-11*H*-benzo[4,5]thieno[3,2-*b*]thiochromene 10,10-dioxide (5f): white solid; 89% yield; 98% ee; >20:1 dr, $[\alpha]_D^{20}$ = +121.1 (*c* 1.0, CH_2Cl_2); m.p.202.3-203.1 ℃; The ee was determined by HPLC analysis using a Chiralpak OD-H column (50/50 hexane/i-PrOH; flow rate: 1.0 mL/min; λ = 254 nm; t_{major} = 16.13 min, t_{minor} = 5.85 min); ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.04-7.86 (m, 3H), 7.76 (d, *J* = 7.2 Hz, 2H), 7.52 (m, 4H), 7.39 (d, *J* = 7.7 Hz, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 6.59 (s, 1H), 5.12 (d, *J* = 9.1 Hz, 1H), 5.03 (d, *J* = 8.6 Hz, 1H), 4.02 (t, *J* = 8.8 Hz, 1H), 2.38 (s, 3H). ^{13}C NMR (100 MHz,

DMSO-d_6) δ 146.0, 141.5, 138.9, 138.2, 137.2, 135.5, 129.4, 129.3, 129.1, 128.9, 128.5, 128.0, 127.3, 125.8, 125.7, 122.1, 99.6, 69.2, 68.1, 44.6, 21.2; HRMS (ESI) Calcd. for $C_{22}H_{18}NaO_3S_2$ $[M+Na]^+$: 417.0590; found: 417.0588.

7. Scale-up Experiment



To a reaction tube were added the 3-formyl-2-mercapto-indole **1a** (2.5 mmol, 1.0 equiv.), the benzo[*b*]thiophene 1,1-dioxide **2a** (2.75 mmol, 1.1 equiv.), catalyst **D** (0.25 mmol) and toluene (12.5 mL). The reaction mixture was stirred at 0 °C for 48 h. the reaction mixture was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to afford the desired product **3a** (1.087 g, 98% yield, >20:1 dr and 99% ee).

To a reaction tube were added the 2-mercaptobenzaldehyde **4a** (1.1 mmol, 1.0 equiv.), benzo[*b*]thiophene 1,1-dioxide **2a** (1 mmol, 1.1 equiv.), catalyst **D** (0.1 mmol) and toluene (5 mL). The reaction mixture was stirred at -20 °C for 5 h. the reaction mixture was directly purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford the desired product **5 a**(0.292 g, 96% yield, >20:1 dr and 93% ee).

8. General experimental procedures for in vitro cytotoxicity assay

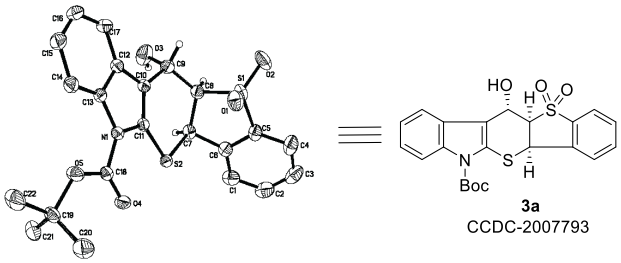
Human leukemia cells K562 were purchased from Chinese Academy of Sciences, Kunming Cell Bank and Chinese Academy of Sciences, Shanghai Cell Bank respectively. The cells were cultured in RPMI-1640 medium (GIBICO, USA), supplemented with 10% fetal bovine serum (Hyclone, USA) and Penicillin-Streptomycin (respectively 100 U/mL) in 5% CO_2 at 37 ℃. The cytotoxicity assay was performed according to the MTT method in 96-well microplates. Briefly, 5000 cells were seeded into each well of 96-well cell culture plates and allowed to grow for 24 h before the drug is added. The K562 tumor cell line was exposed to compounds (**3a**, **3d**, **3e**, **3g**, **3h**, **3i**, **3j**, **3l**, **3o**, **3q**, **3r** and **3t**) at the concentrations of 1, 2, 4, 8 and 20 μmol·L^{-1} in triplicates for 48 h, comparable to cisplatin (Aladdin, China). Then the MTT reagent was added to reaction with the cancer cells for 4 hours. At least, measure the OD value at 490 wavelengths. The average 50% inhibitory concentration (IC_{50}) of all the compounds is calculated by IBM SPSS Statistics (version 19). Each concentration was analyzed in triplicate at least, and the whole experiment was repeated three times.

Table 1. Cell inhibitory assay of target products in human leukemia cells K562

Compound	IC_{50} (uM)	Compound	IC_{50} (uM)	Compound	IC_{50} (uM)
3a	20.31	**3h**	20.95	**3o**	21.71
3d	10.31	**3i**	12.04	**3q**	33.31
3e	24.94	**3j**	34.06	**3r**	31.35
3g	17.08	**3l**	20.10	**3t**	32.65

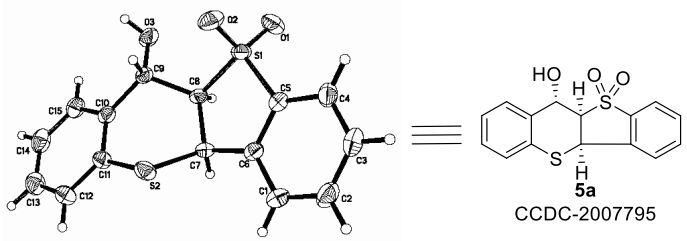
[a]IC_{50} is the concentration of a compound that affords a 50% reduction in cell growth (after 48 h of incubation), expressed as the mean of triplicate experiments. [b]Commercially available broad-spectrum anticancer drug cisplatin as a positive control (IC_{50} = 21.863 uM).

9. X-ray crystal structure of 3a and 5a.



Crystal data and structure refinement for **3a**

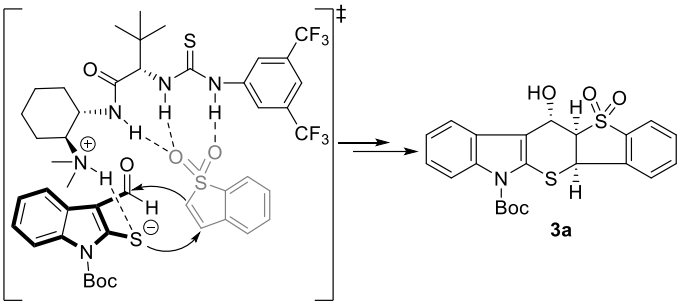
Identification code	**3a**
Empirical formula	$C_{22}H_{21}NO_5S_2$
Formula weight	443.52
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	8.71695(13)
b/Å	13.36161(18)
c/Å	17.6913(2)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2060.55(5)
Z	4
ρ_{calc}g/cm^3	1.430
μ/mm^{-1}	2.645
F(000)	928.0
Crystal size/mm^3	0.15 × 0.13 × 0.1
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.292 to 142.13
Index ranges	$-10 \le h \le 10$, $-16 \le k \le 16$, $-21 \le l \le 21$
Reflections collected	19546
Independent reflections	3953 [R_{int} = 0.0413, R_{sigma} = 0.0272]
Data/restraints/parameters	3953/0/274
Goodness-of-fit on F^2	1.090
Final R indexes [I>=2σ (I)]	R_1 = 0.0368, wR_2 = 0.0982
Final R indexes [all data]	R_1 = 0.0377, wR_2 = 0.0996
Largest diff. peak/hole / e Å^{-3}	0.47/-0.24
Flack parameter	0.013(9)



Crystal data and structure refinement for **5a**

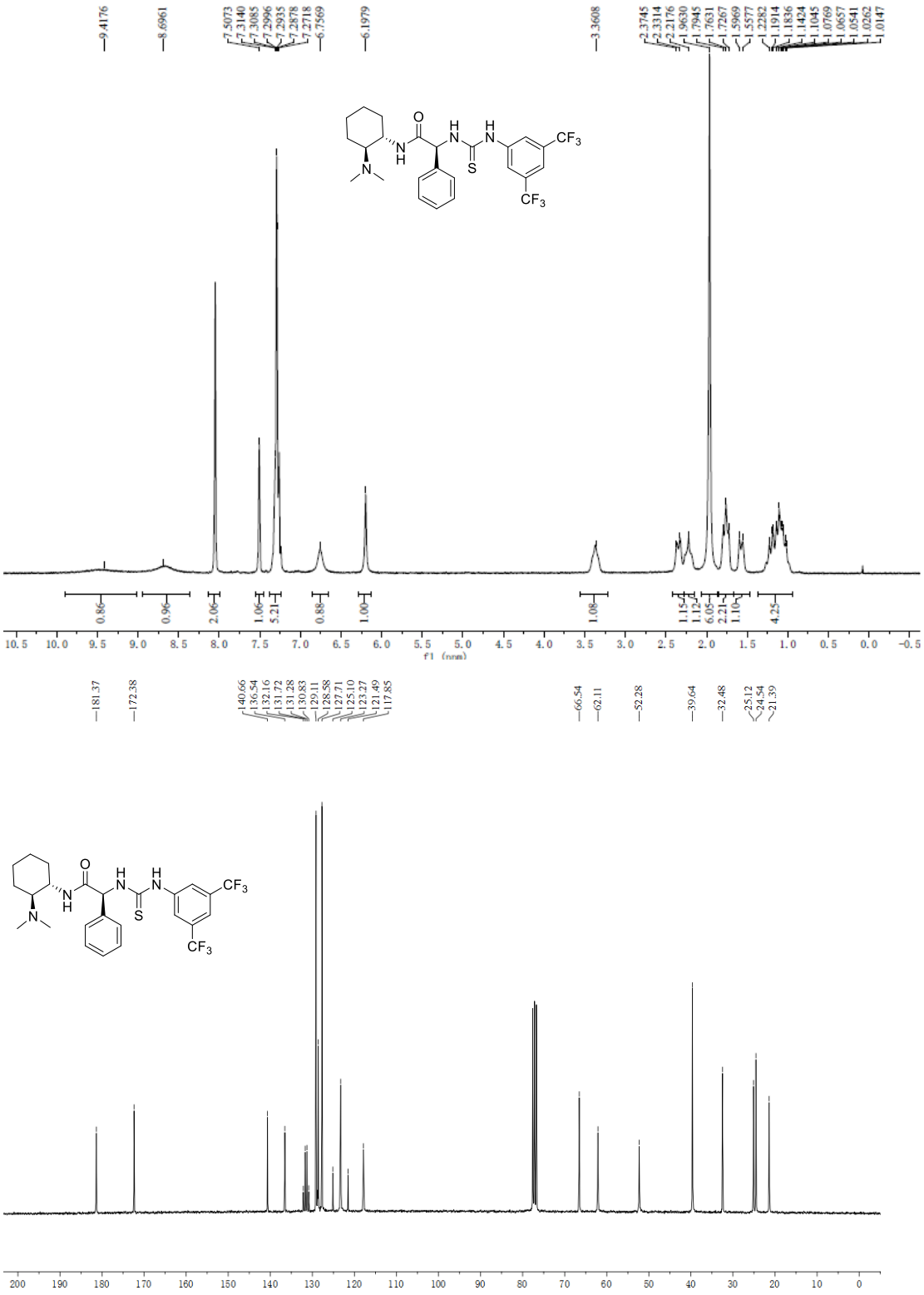
Identification code	**5a**
Empirical formula	$C_{15}H_{12}O_3S_2$
Formula weight	304.37
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	7.8266(4)
b/Å	13.1360(6)
c/Å	13.1894(5)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	1356.00(10)
Z	4
ρ_{calc}g/cm^3	1.491
μ/mm^{-1}	3.601
F(000)	632.0
Crystal size/mm^3	0.2 × 0.16 × 0.1
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	9.502 to 134.12
Index ranges	$-5 \le h \le 9$, $-13 \le k \le 15$, $-14 \le l \le 15$
Reflections collected	4921
Independent reflections	2433 [R_{int} = 0.0297, R_{sigma} = 0.0426]
Data/restraints/parameters	2433/0/182
Goodness-of-fit on F^2	1.063
Final R indexes [I>=2σ (I)]	R_1 = 0.0399, wR_2 = 0.0977
Final R indexes [all data]	R_1 = 0.0451, wR_2 = 0.1030
Largest diff. peak/hole / e Å^{-3}	0.23/-0.29
Flack parameter	-0.010(15)

10. Proposed transition state for the enantioselective tandem reaction

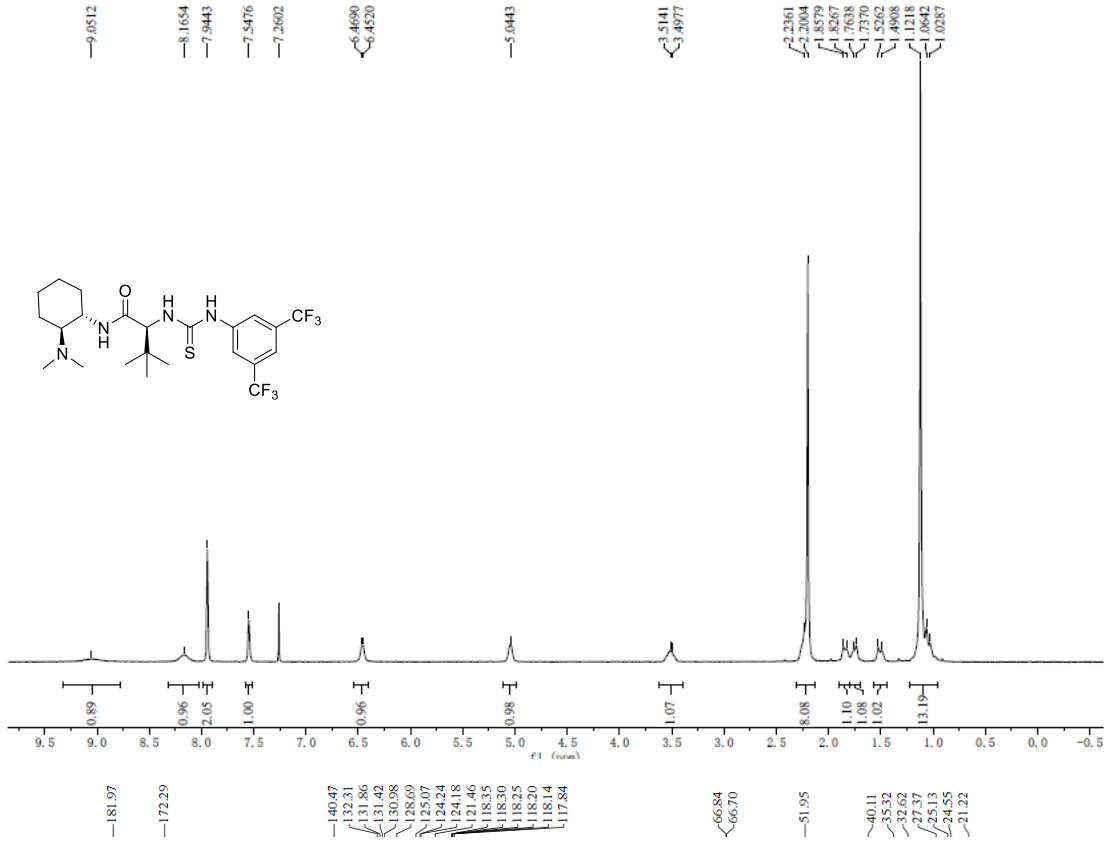


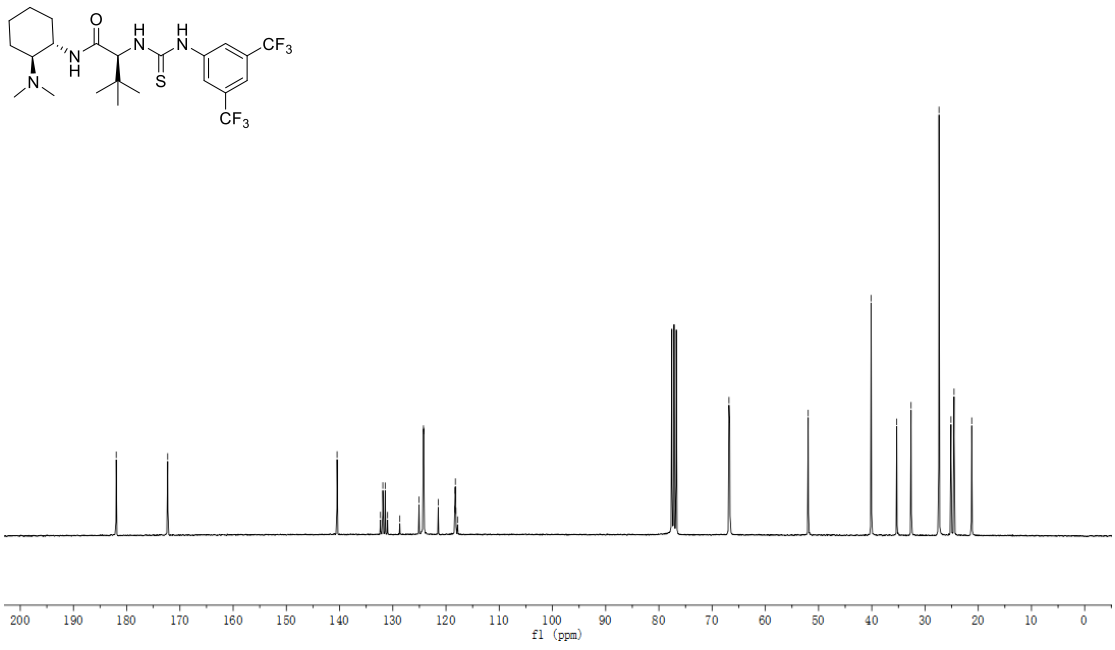
11. ^{1}H, ^{13}C NMR, spectra for catalysts C and D

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



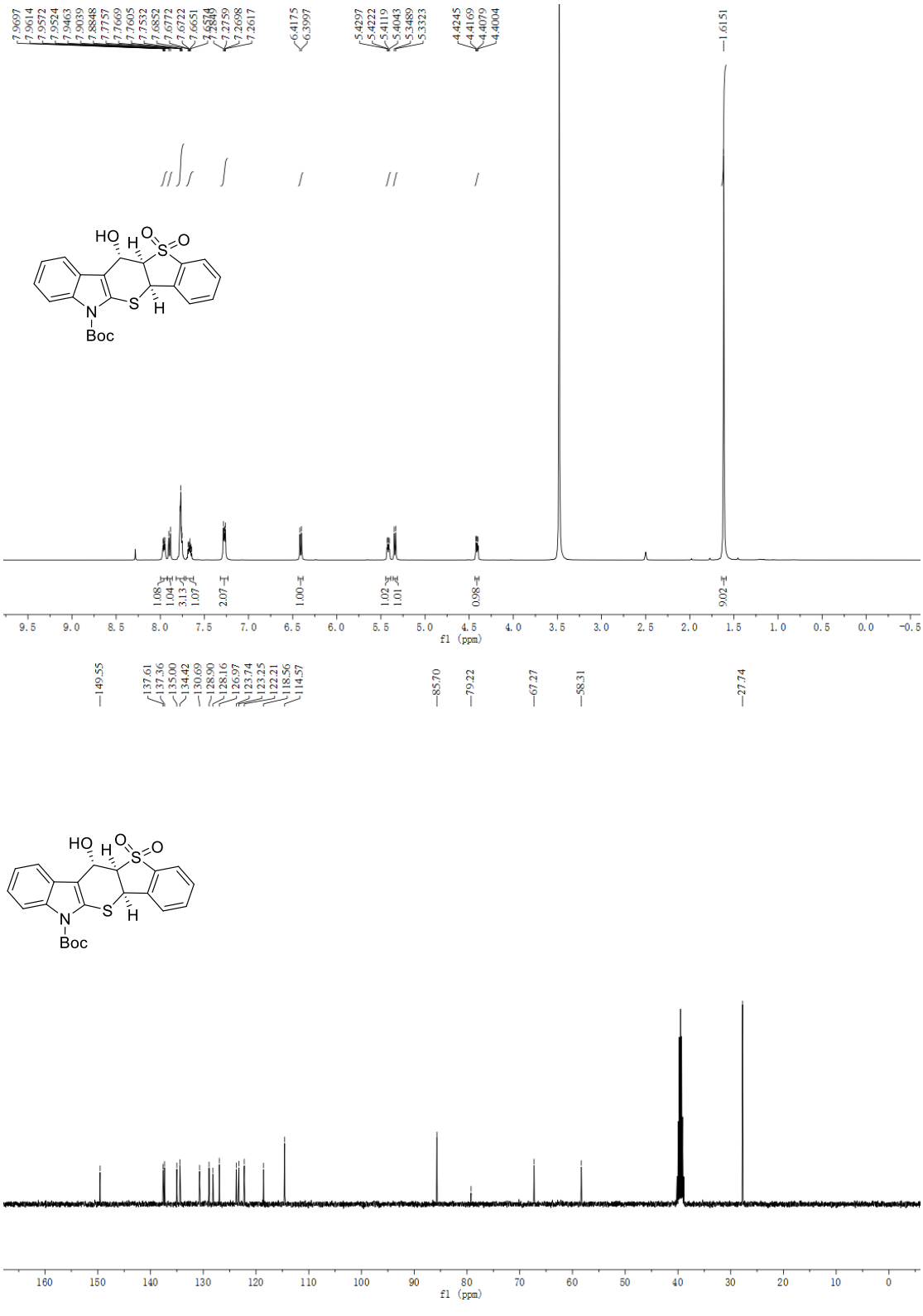
^{1}H and ^{13}C NMR of catalyst **D**



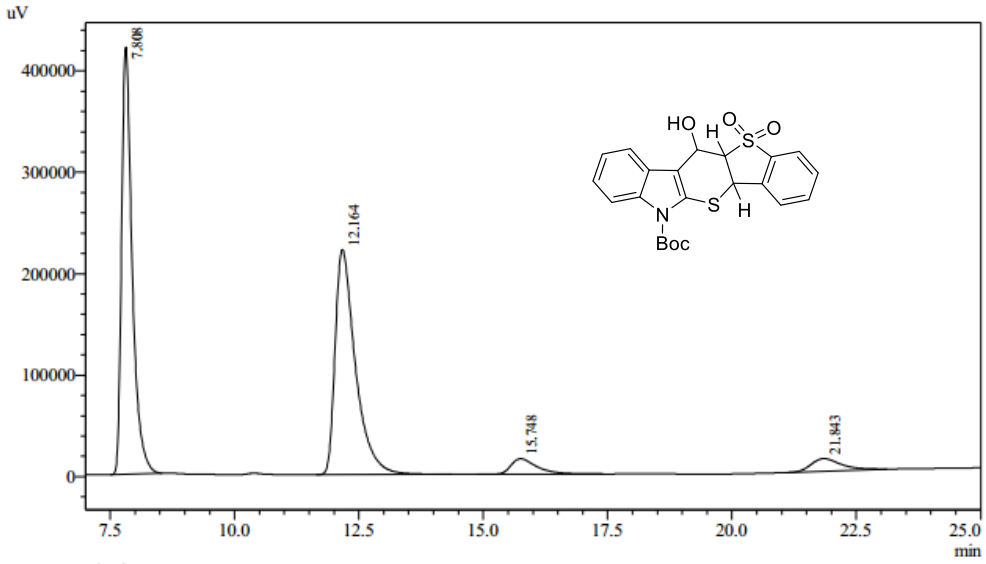


12. ^{1}H, ^{13}C NMR, and HPLC spectra for compounds 3a-y, and compounds 5a-g

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



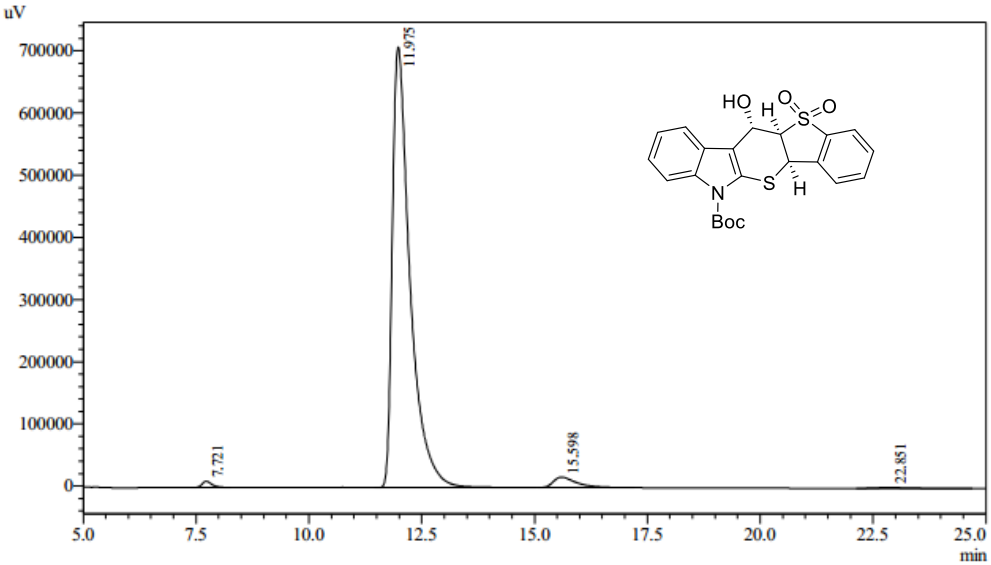
HPLC of **3a**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.808	6245443	421037	45.826	62.785
2	12.164	6304549	221966	46.260	33.099
3	15.748	552266	15165	4.052	2.261
4	21.843	526261	12437	3.861	1.855
Total		13628519	670605	100.000	100.000

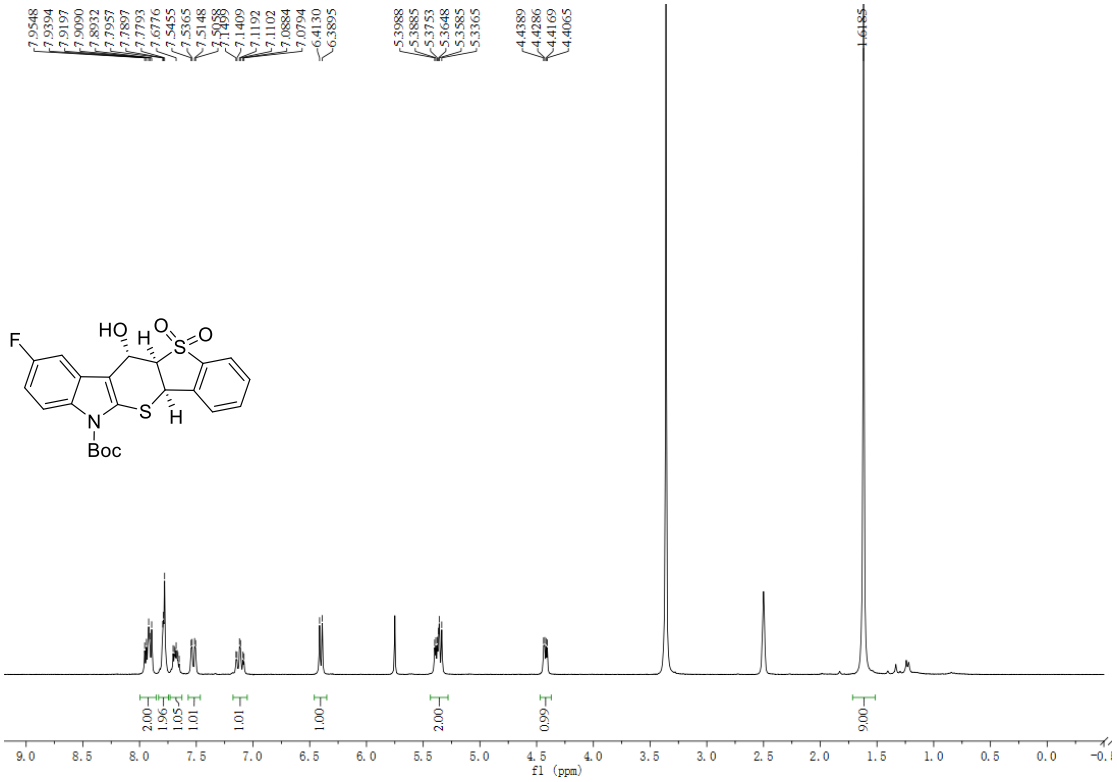


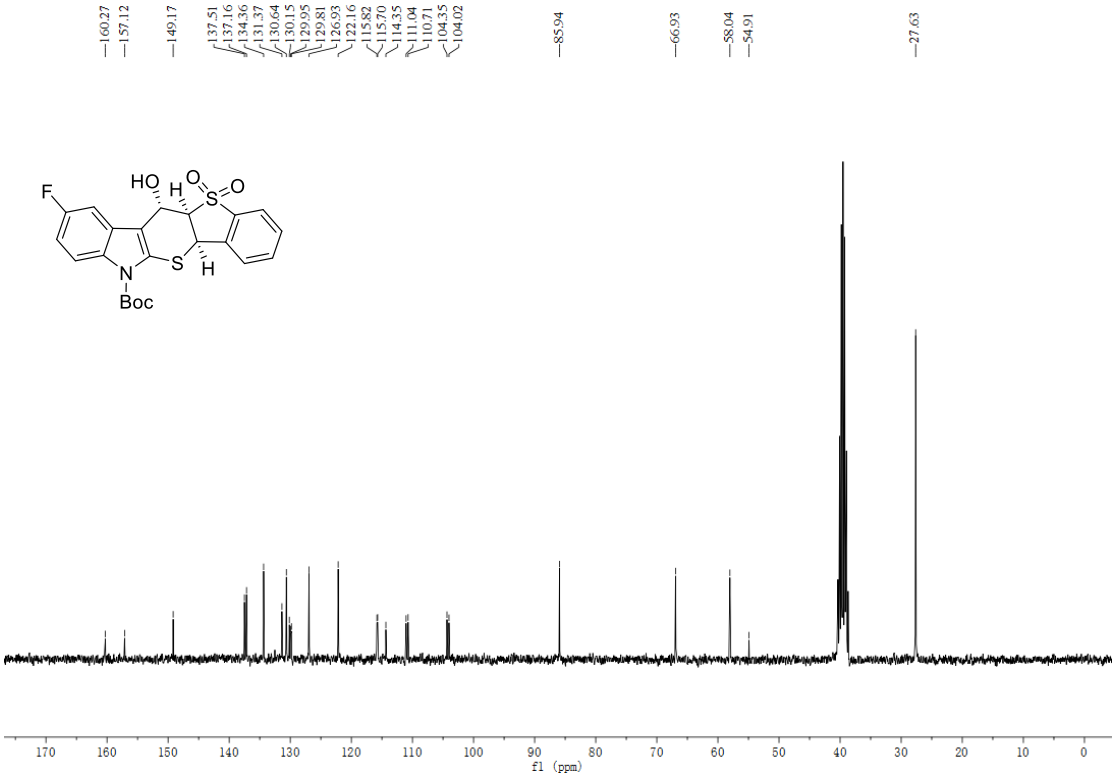
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

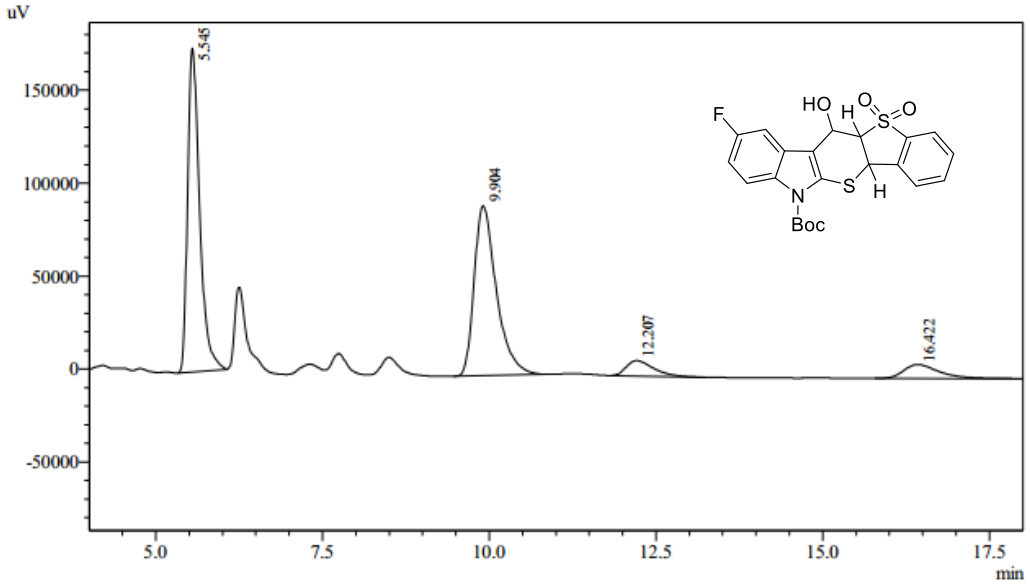
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.721	148335	10060	0.735	1.365
2	11.975	19364251	708622	95.931	96.154
3	15.598	608150	16862	3.013	2.288
4	22.851	64962	1422	0.322	0.193
Total		20185697	736966	100.000	100.000

^{1}H and ^{13}C NMR of **3b**





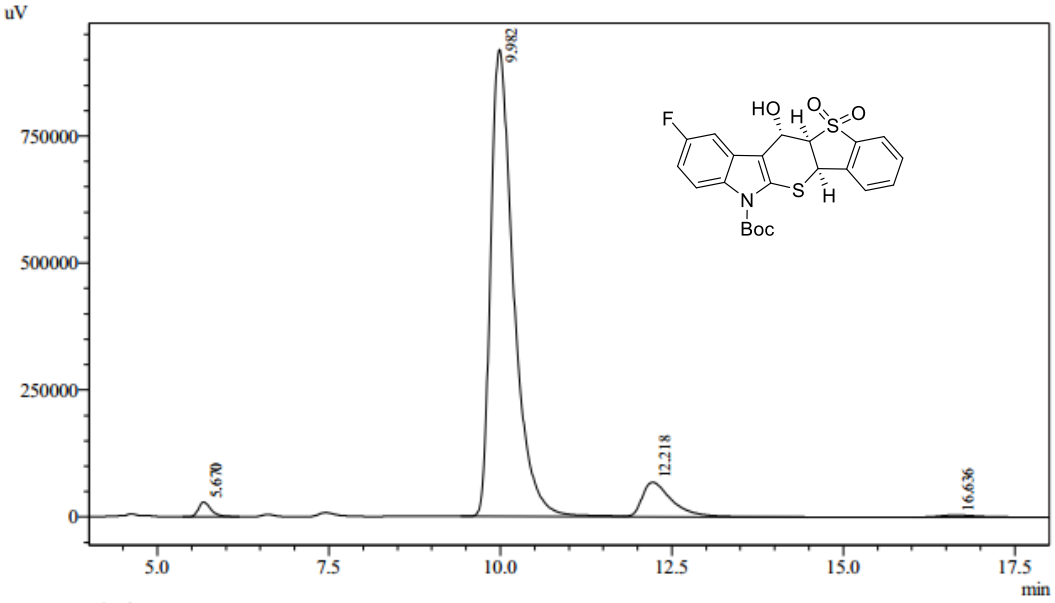
HPLC of **3b**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.545	2183743	174147	45.238	61.899
2	9.904	2126927	91459	44.061	32.508
3	12.207	239232	8263	4.956	2.937
4	16.422	277290	7472	5.744	2.656
Total		4827192	281341	100.000	100.000

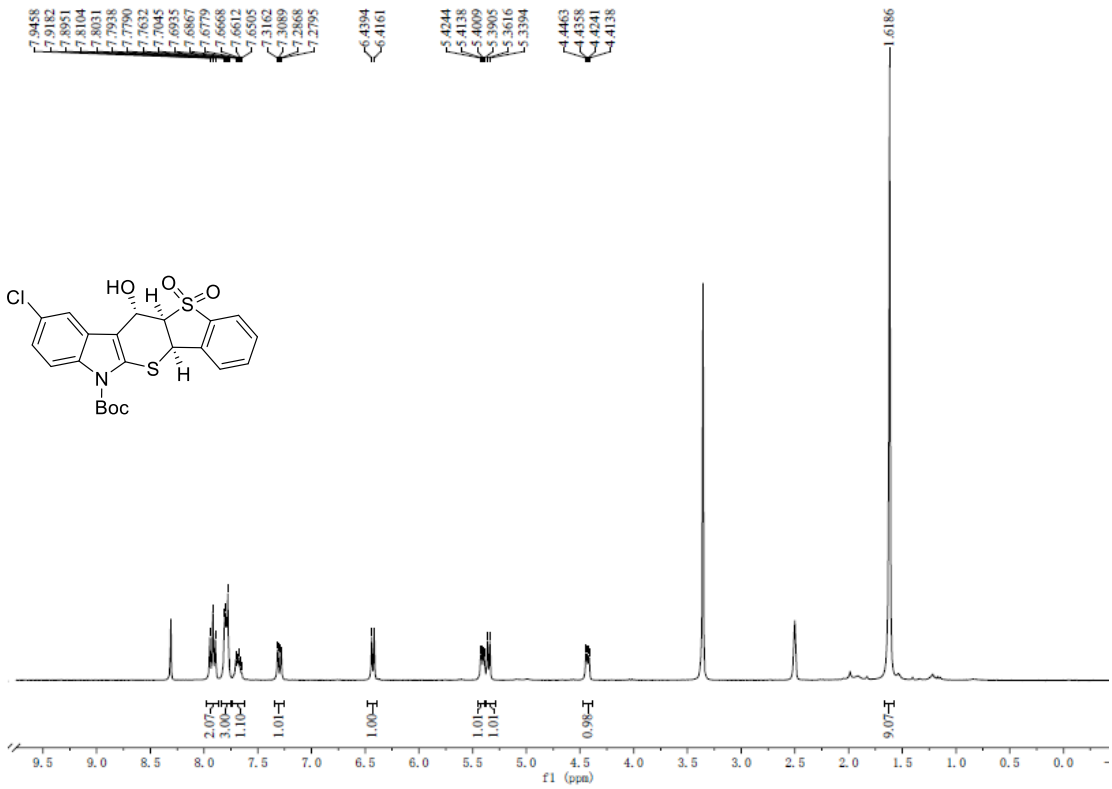


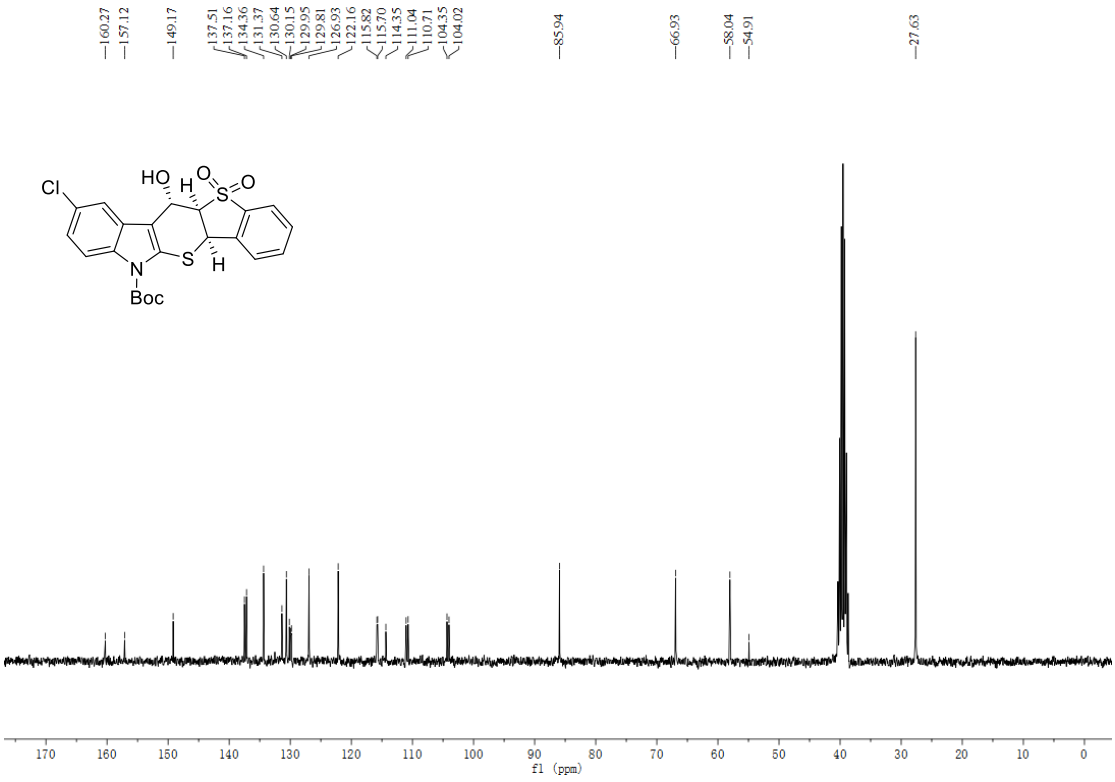
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

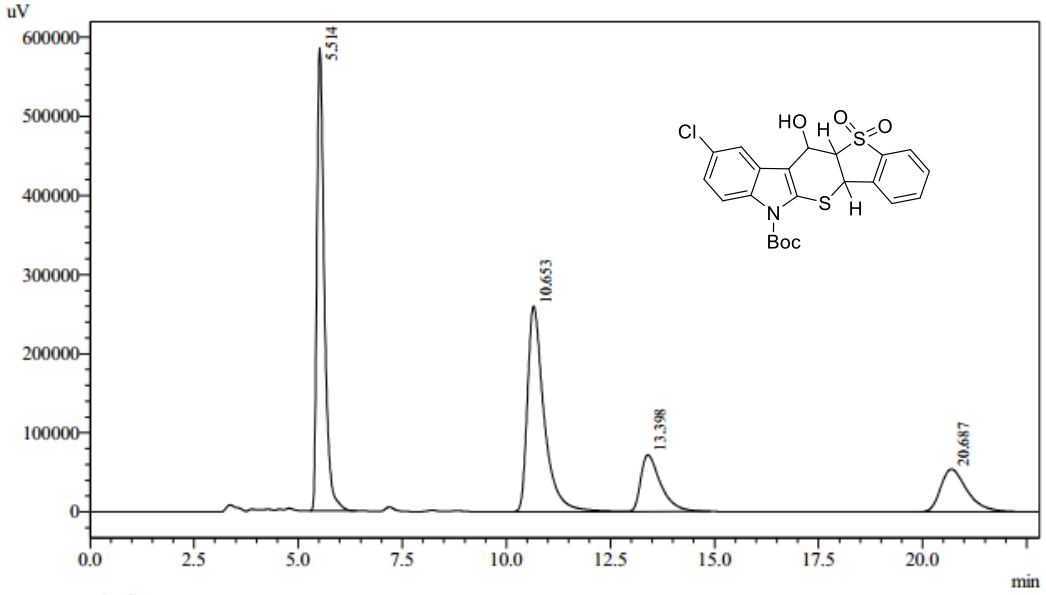
Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.670	364314	28767	1.523	2.820
2	9.982	21368667	919304	89.326	90.132
3	12.218	2039181	67818	8.524	6.649
4	16.636	149871	4067	0.626	0.399
Total		23922034	1019956	100.000	100.000

^{1}H and ^{13}C NMR of **3c**





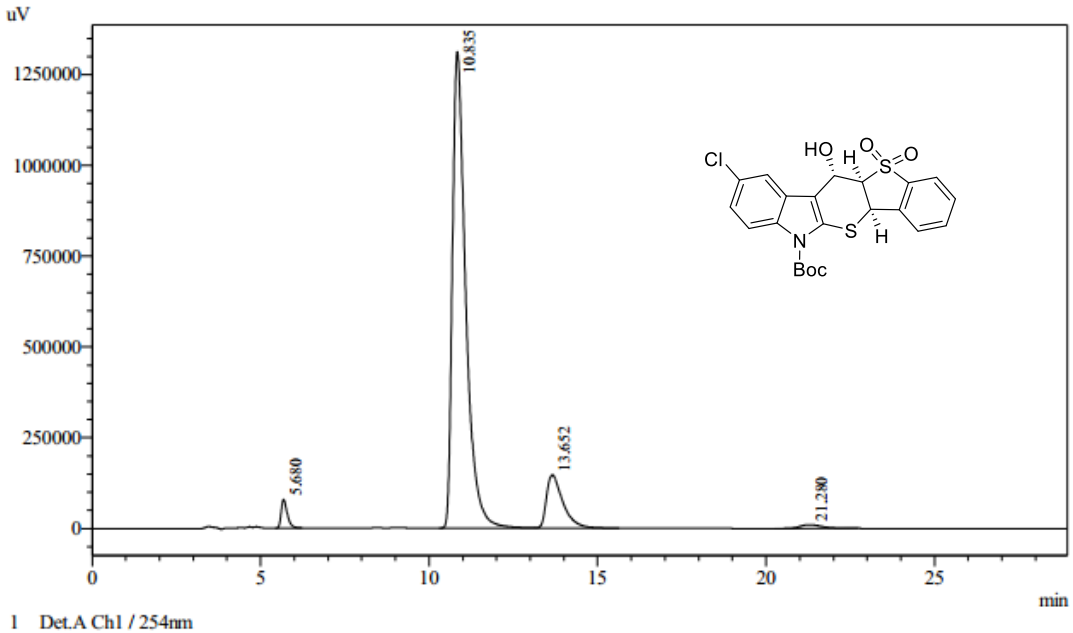
HPLC of **3c**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.514	7296270	585529	37.727	60.295
2	10.653	7237856	259759	37.425	26.749
3	13.398	2385541	71738	12.335	7.387
4	20.687	2419956	54082	12.513	5.569
Total		19339623	971108	100.000	100.000

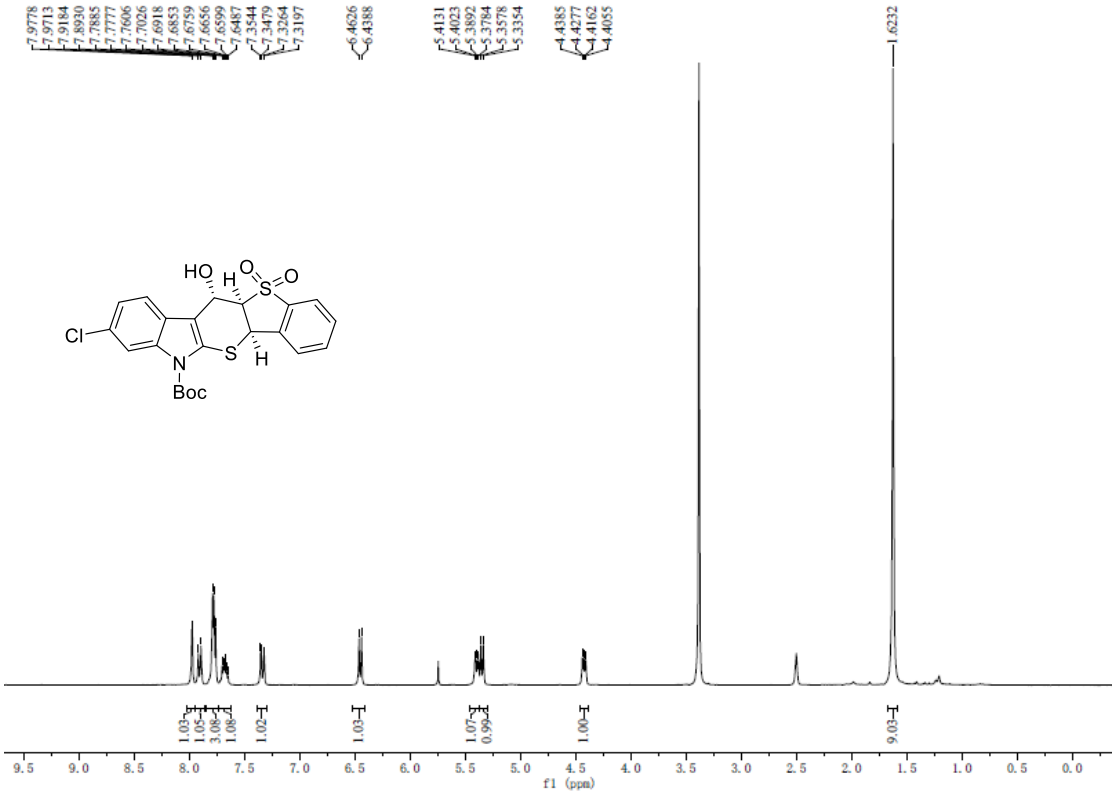


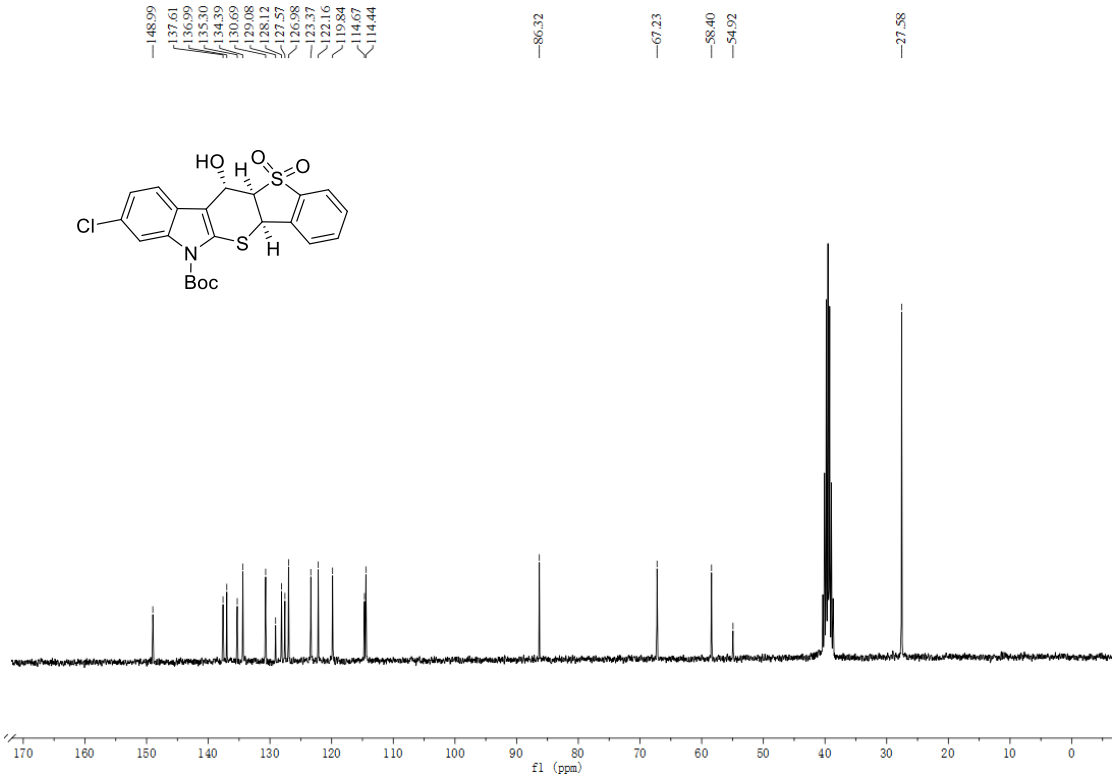
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

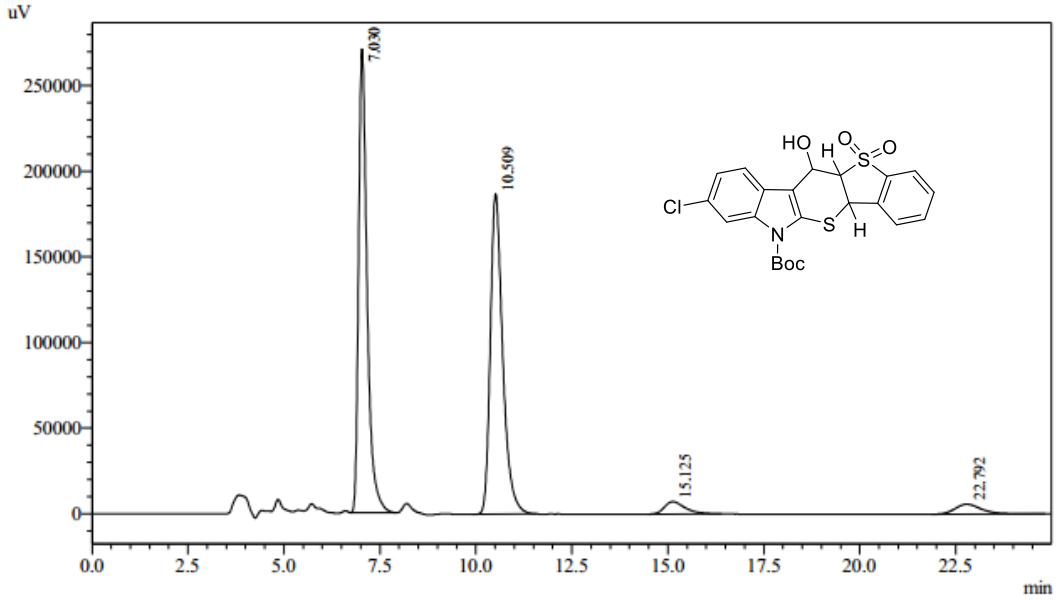
Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.680	1005362	79055	2.362	5.105
2	10.835	36101435	1312180	84.818	84.741
3	13.652	4981935	146713	11.705	9.475
4	21.280	474468	10501	1.115	0.678
Total		42563199	1548450	100.000	100.000

^{1}H and ^{13}C NMR of **3d**





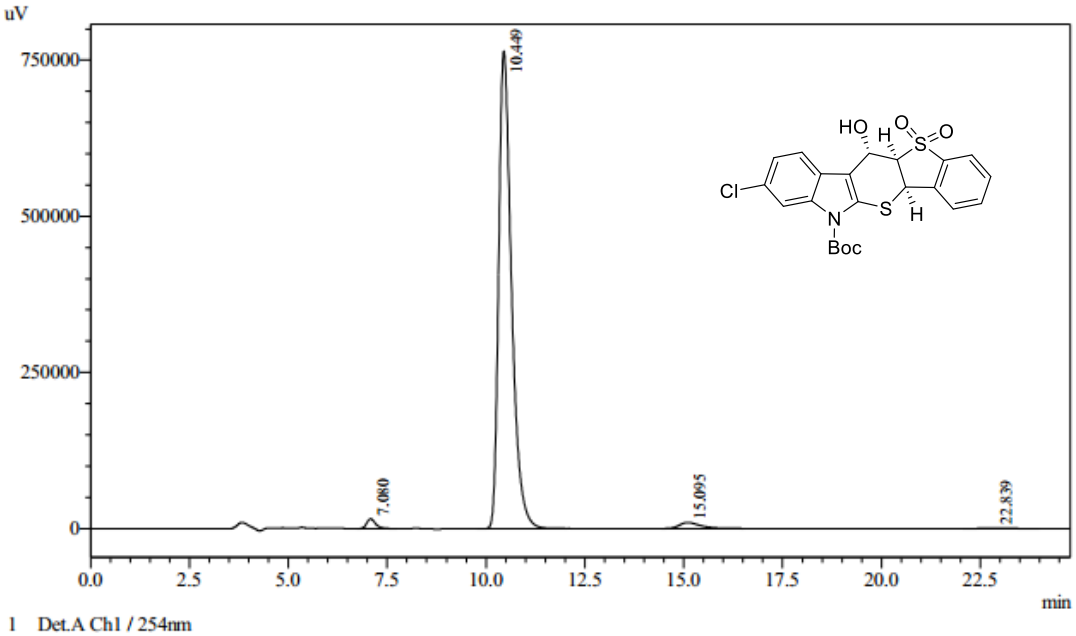
HPLC of **3d**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.030	4201131	270838	47.000	57.534
2	10.509	4193244	186914	46.912	39.706
3	15.125	271707	7236	3.040	1.537
4	22.792	272434	5757	3.048	1.223
Total		8938516	470744	100.000	100.000

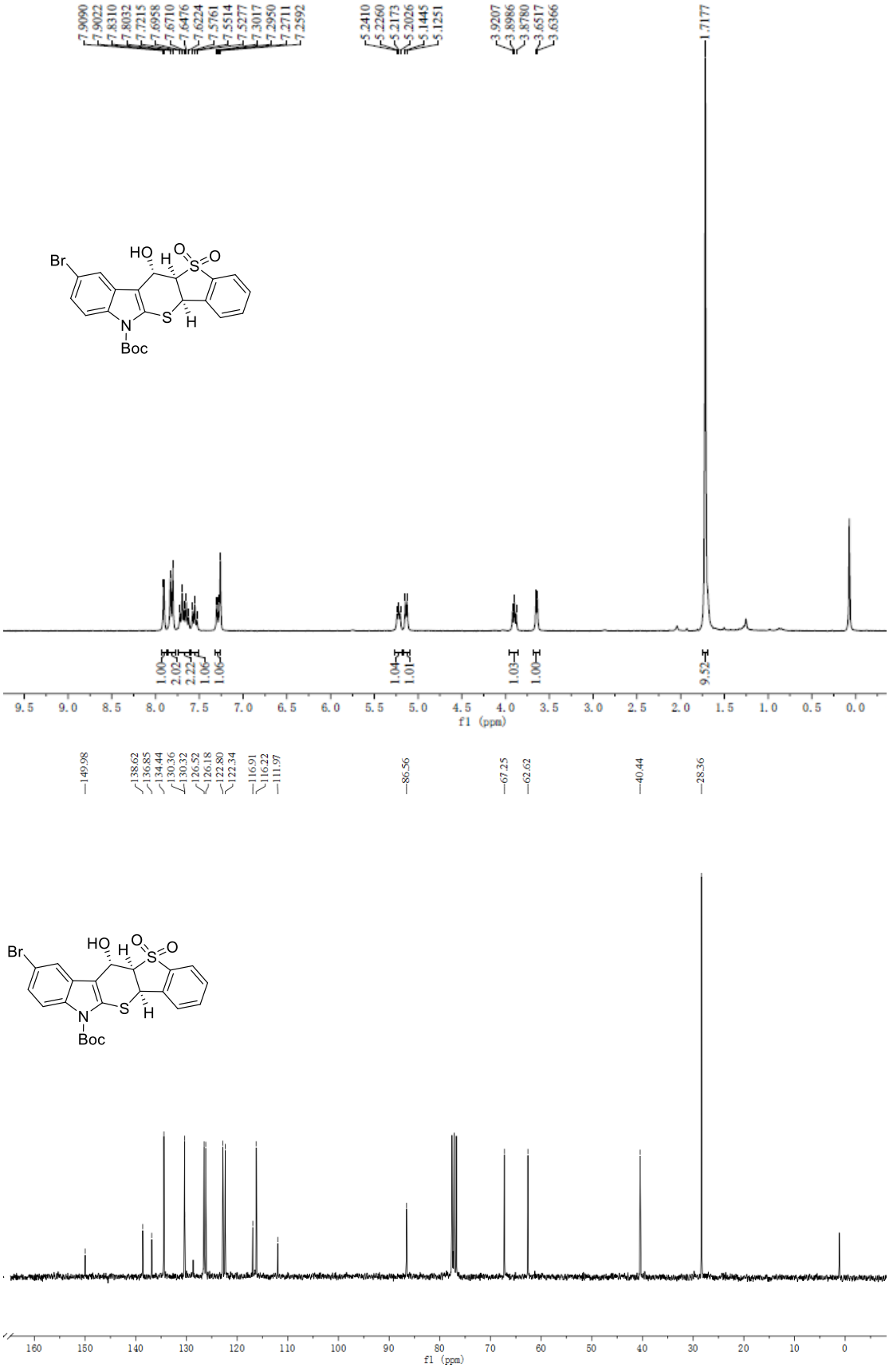


1 Det.A Ch1 / 254nm

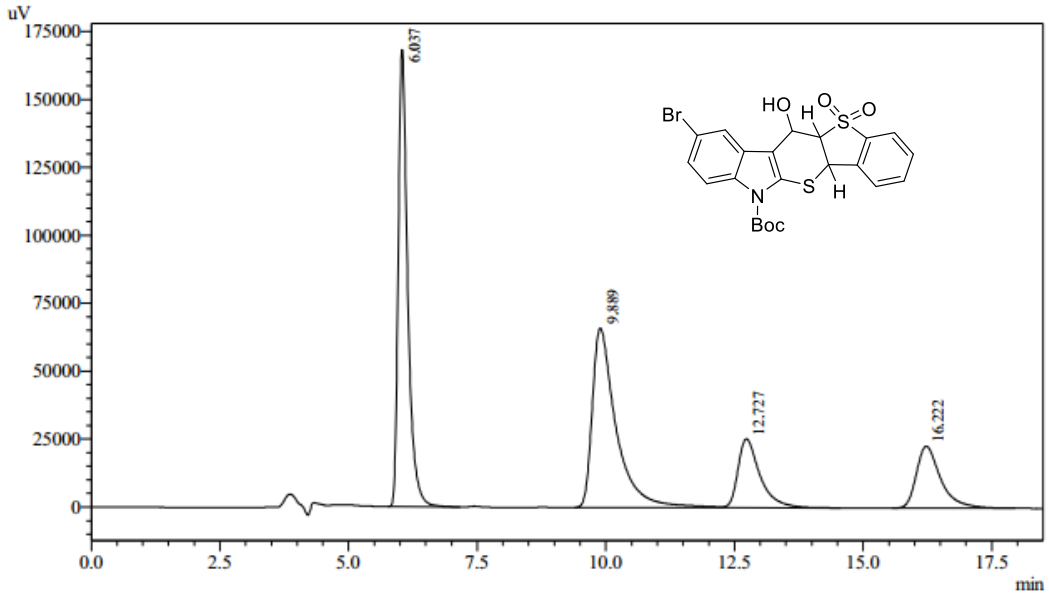
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.080	249509	15774	1.397	1.995
2	10.449	17216978	764683	96.413	96.709
3	15.095	360507	9558	2.019	1.209
4	22.839	30575	687	0.171	0.087
Total		17857569	790701	100.000	100.000

^{1}H and ^{13}C NMR of **3e**



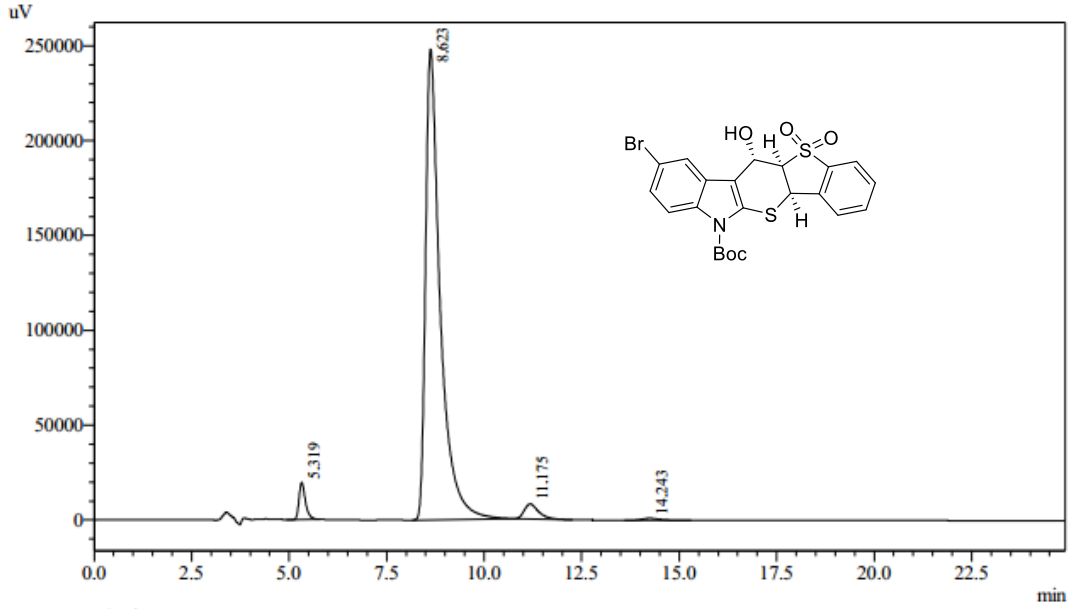
HPLC of **3e**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.037	2157799	168164	37.253	59.577
2	9.889	2128333	65990	36.744	23.379
3	12.727	756417	25336	13.059	8.976
4	16.222	749746	22775	12.944	8.069
Total		5792294	282265	100.000	100.000

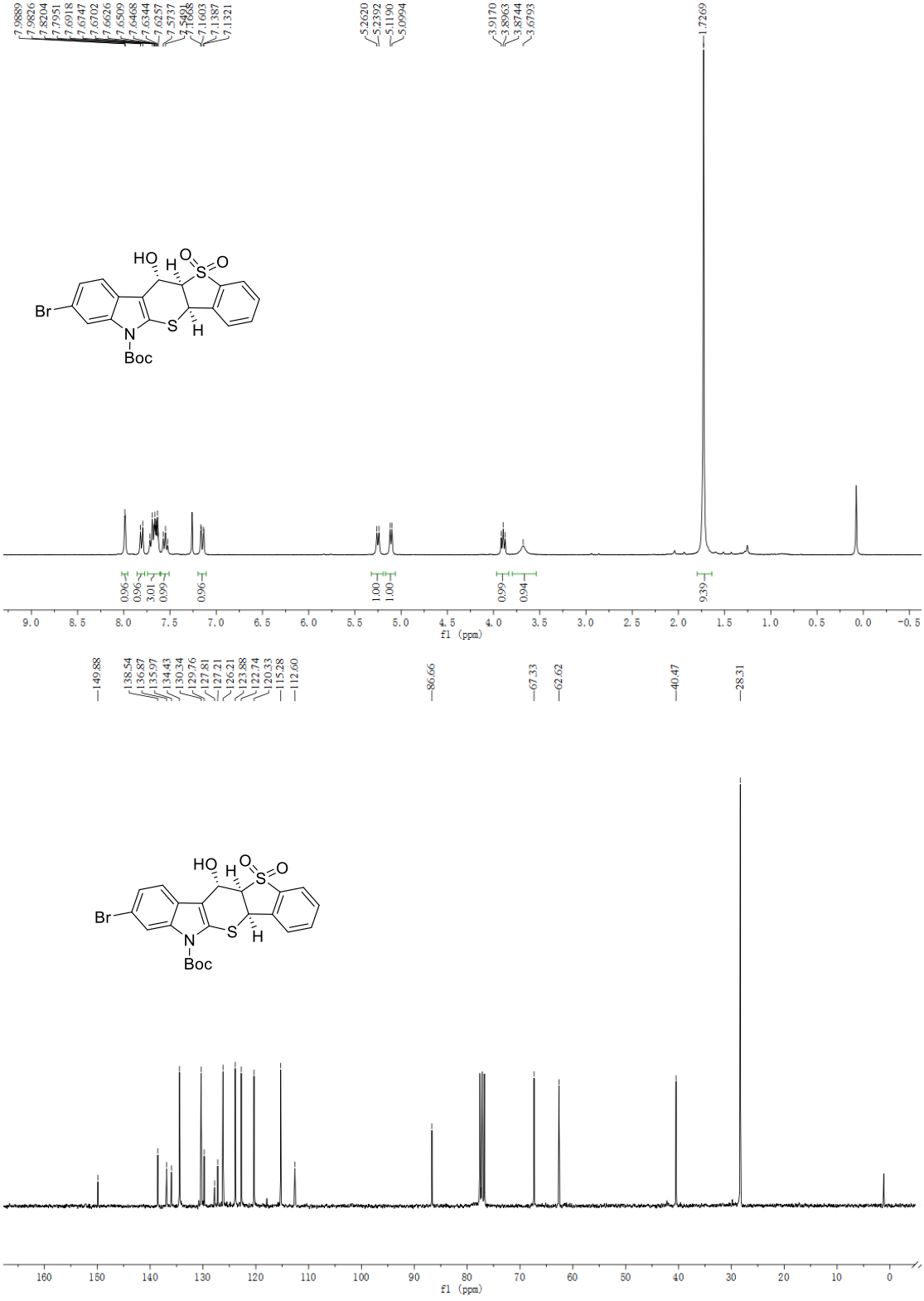


1 Det.A Ch1 / 254nm

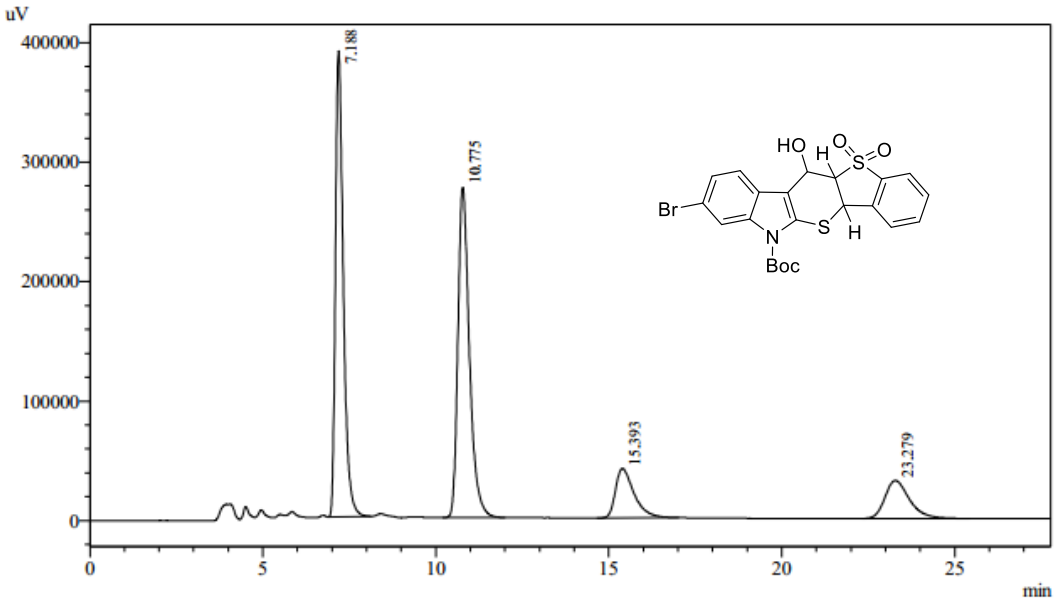
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.319	226733	19698	3.252	7.116
2	8.623	6509417	248118	93.350	89.641
3	11.175	206322	7921	2.959	2.862
4	14.243	30692	1054	0.440	0.381
Total		6973163	276791	100.000	100.000

^{1}H and ^{13}C NMR of **3f**



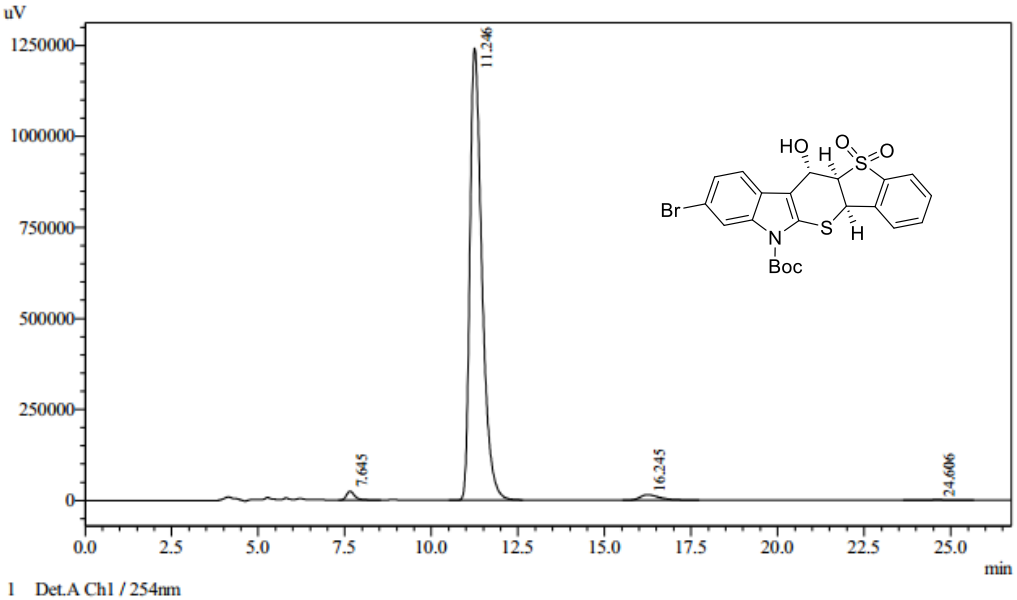
HPLC of **3f**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.188	6197228	390024	39.528	52.756
2	10.775	6360812	276112	40.571	37.348
3	15.393	1543001	41323	9.842	5.590
4	23.279	1577196	31836	10.060	4.306
Total		15678237	739295	100.000	100.000

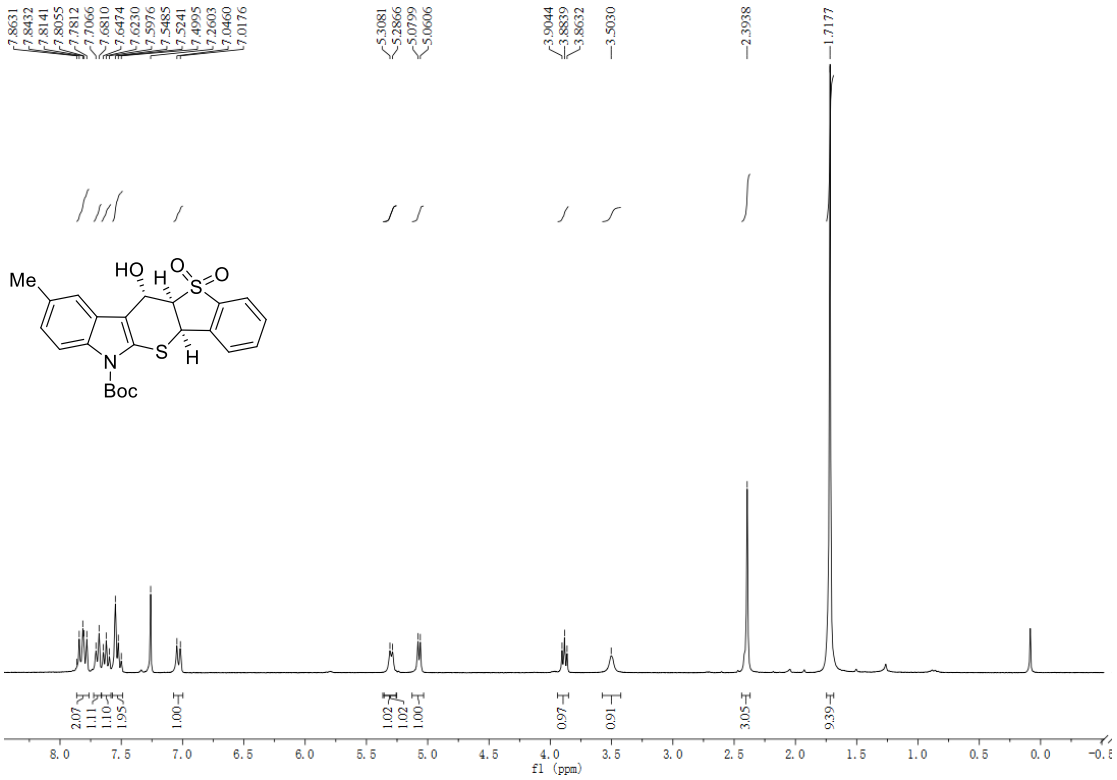


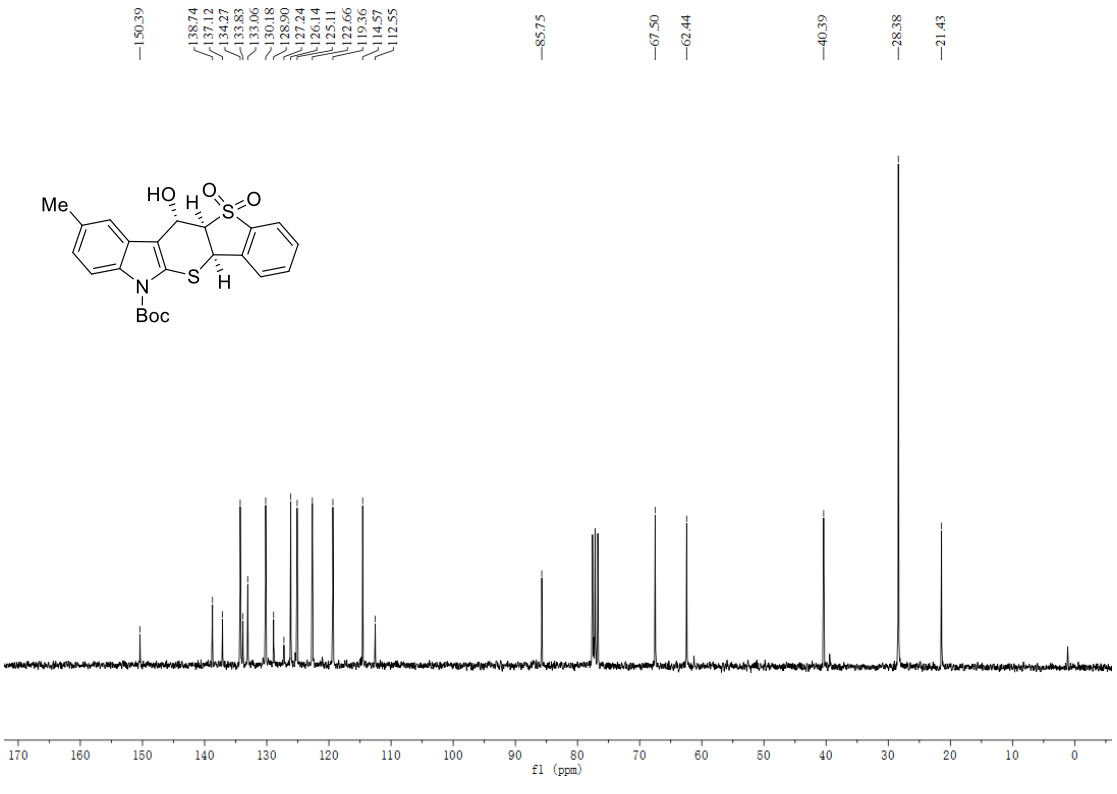
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

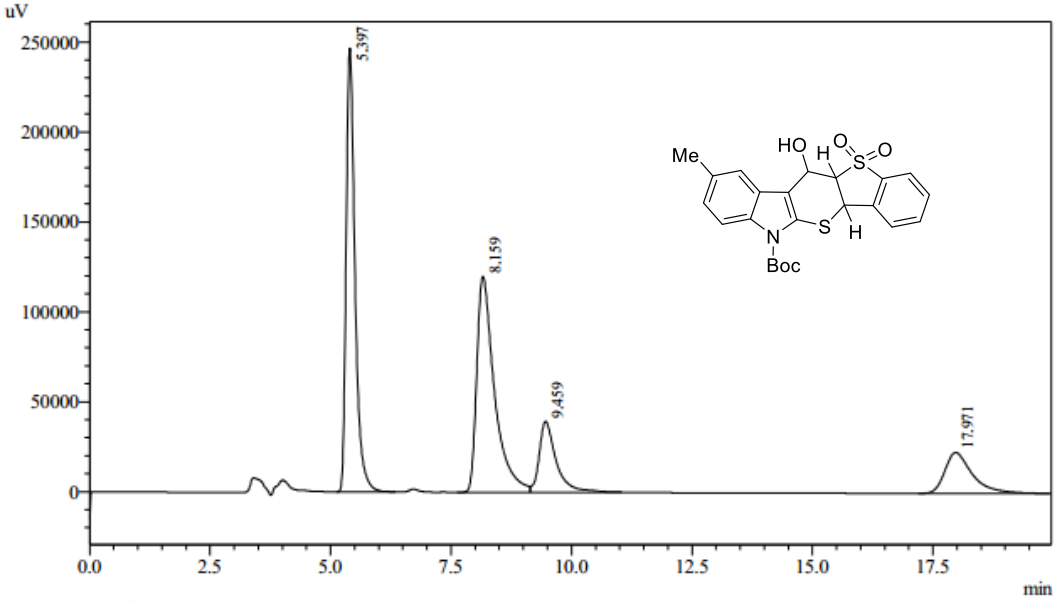
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.645	402573	24504	1.298	1.911
2	11.246	29965004	1241387	96.647	96.836
3	16.245	583198	14921	1.881	1.164
4	24.606	53721	1131	0.173	0.088
Total		31004496	1281943	100.000	100.000

^{1}H and ^{13}C NMR of **3g**





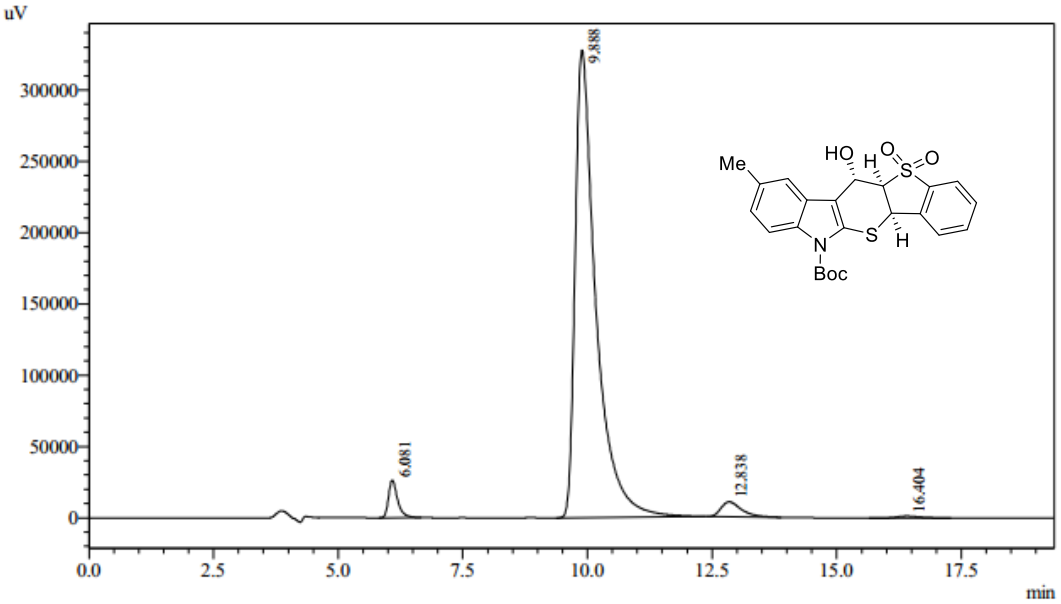
HPLC of **3g**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.397	3140658	246731	38.881	57.513
2	8.159	3065400	120118	37.950	27.999
3	9.459	963519	39441	11.928	9.194
4	17.971	907961	22713	11.241	5.294
Total		8077538	429002	100.000	100.000

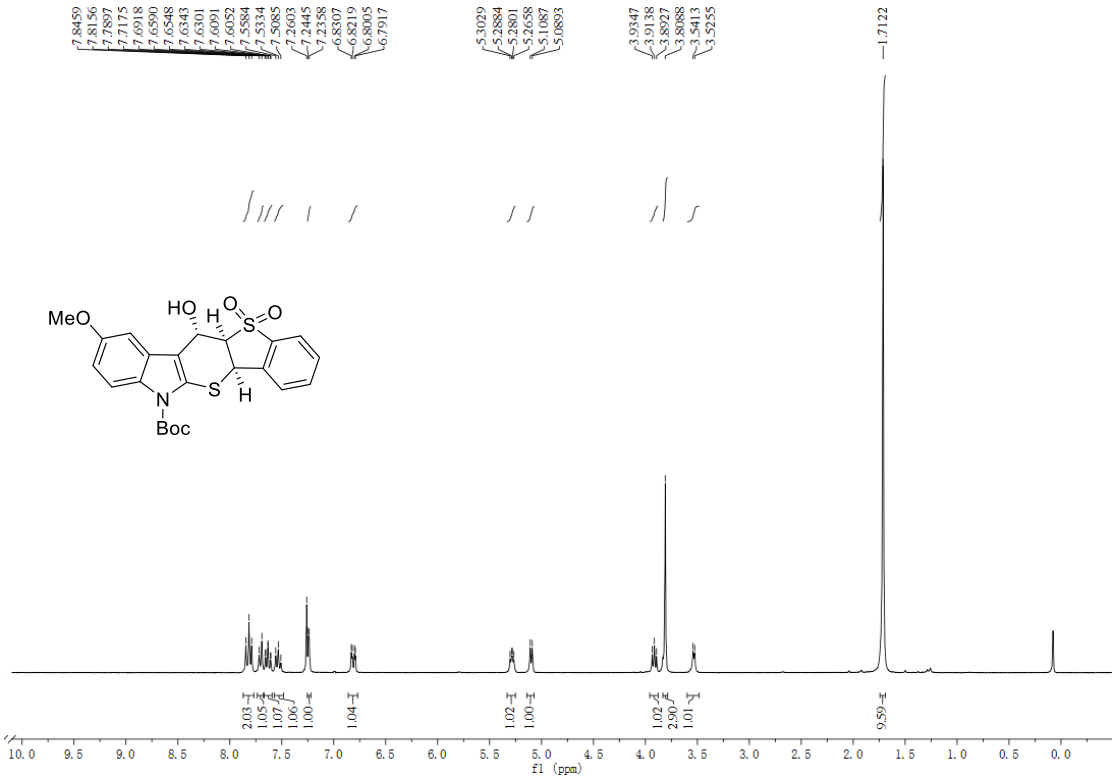


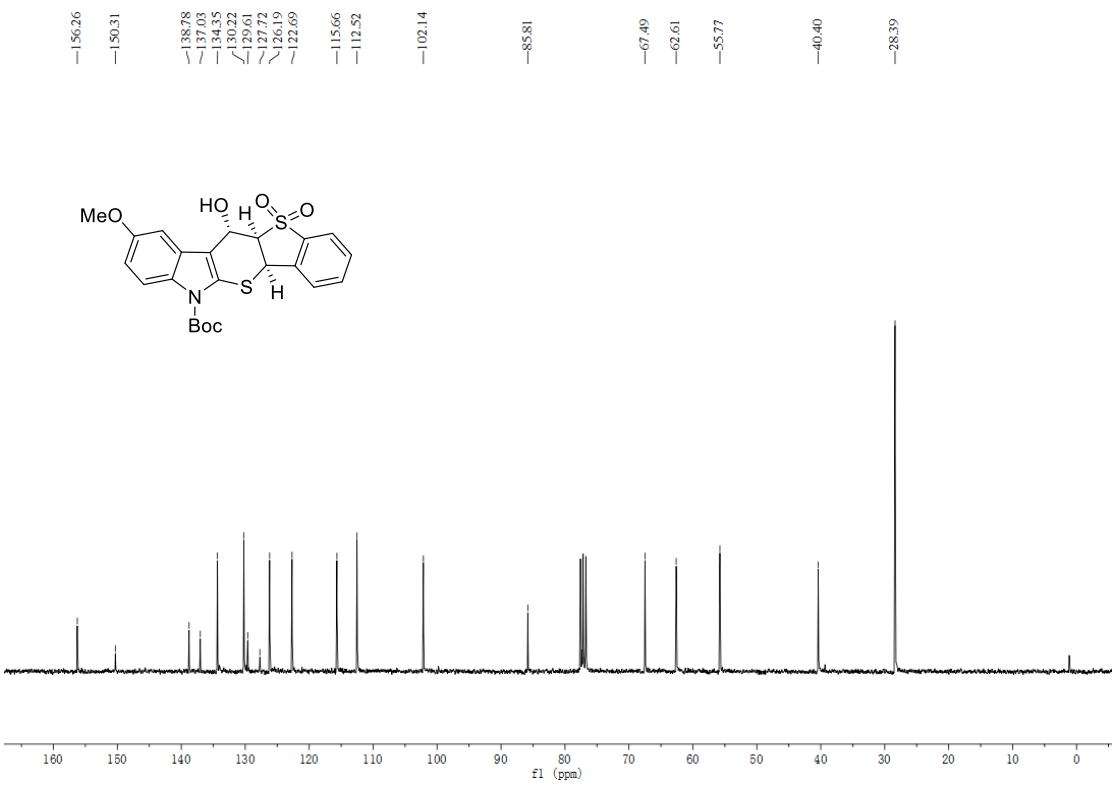
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

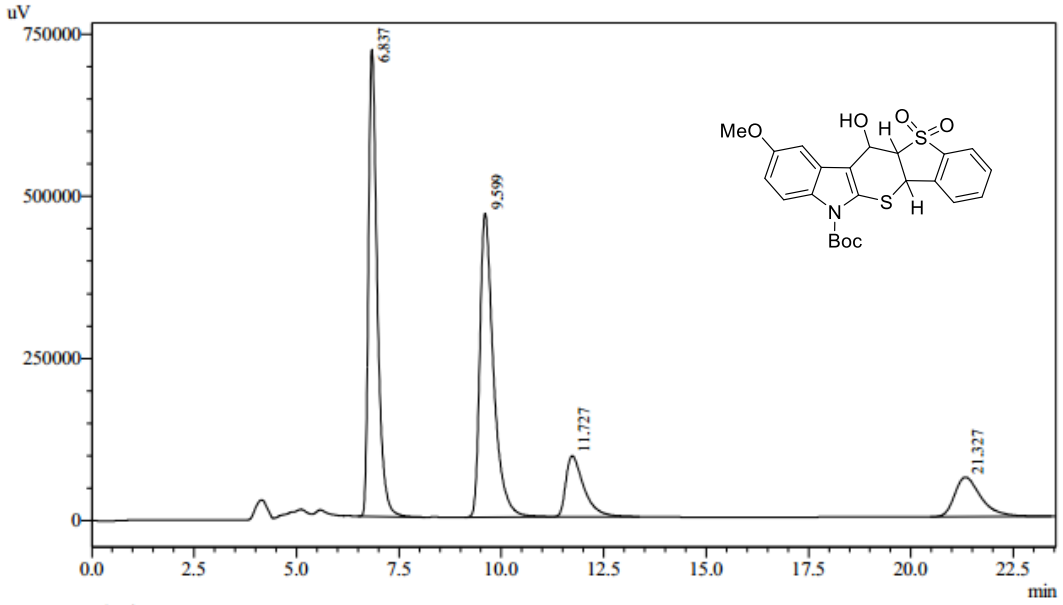
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.081	331268	26324	3.246	7.191
2	9.888	9530437	327894	93.372	89.575
3	12.838	303111	10490	2.970	2.866
4	16.404	42156	1348	0.413	0.368
Total		10206972	366056	100.000	100.000

^{1}H and ^{13}C NMR of **3h**



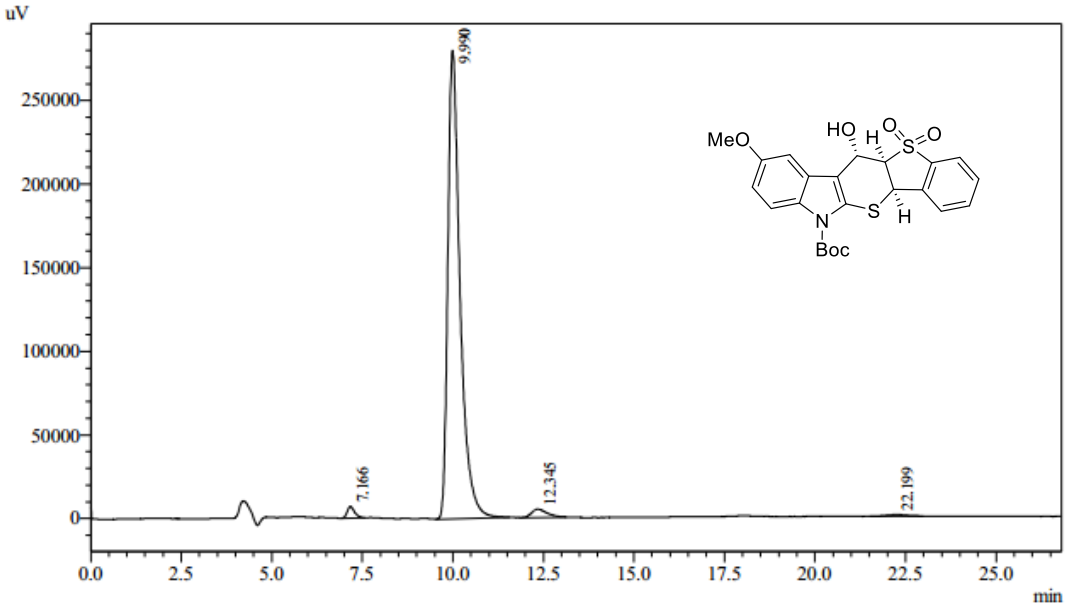


HPLC of **3h**



Detector A Ch1 254nm

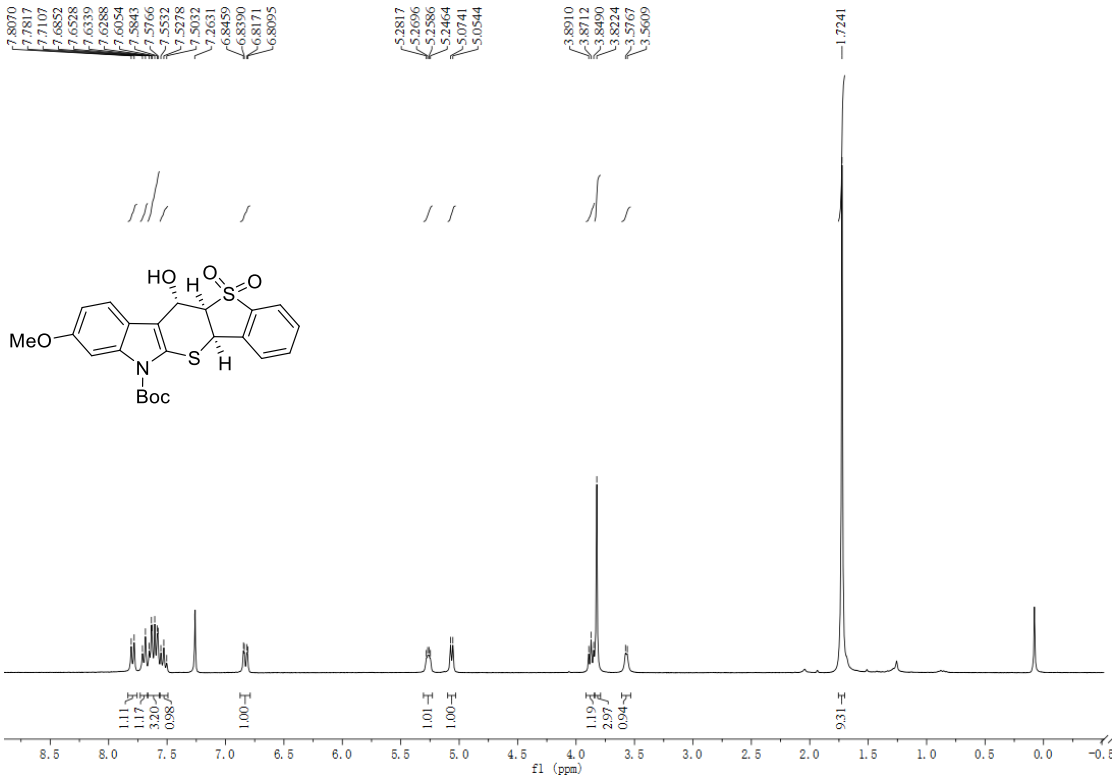
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.837	10820130	720318	39.608	53.584
2	9.599	10859950	468969	39.754	34.886
3	11.727	2902852	94071	10.626	6.998
4	21.327	2734780	60930	10.011	4.532
Total		27317713	1344287	100.000	100.000

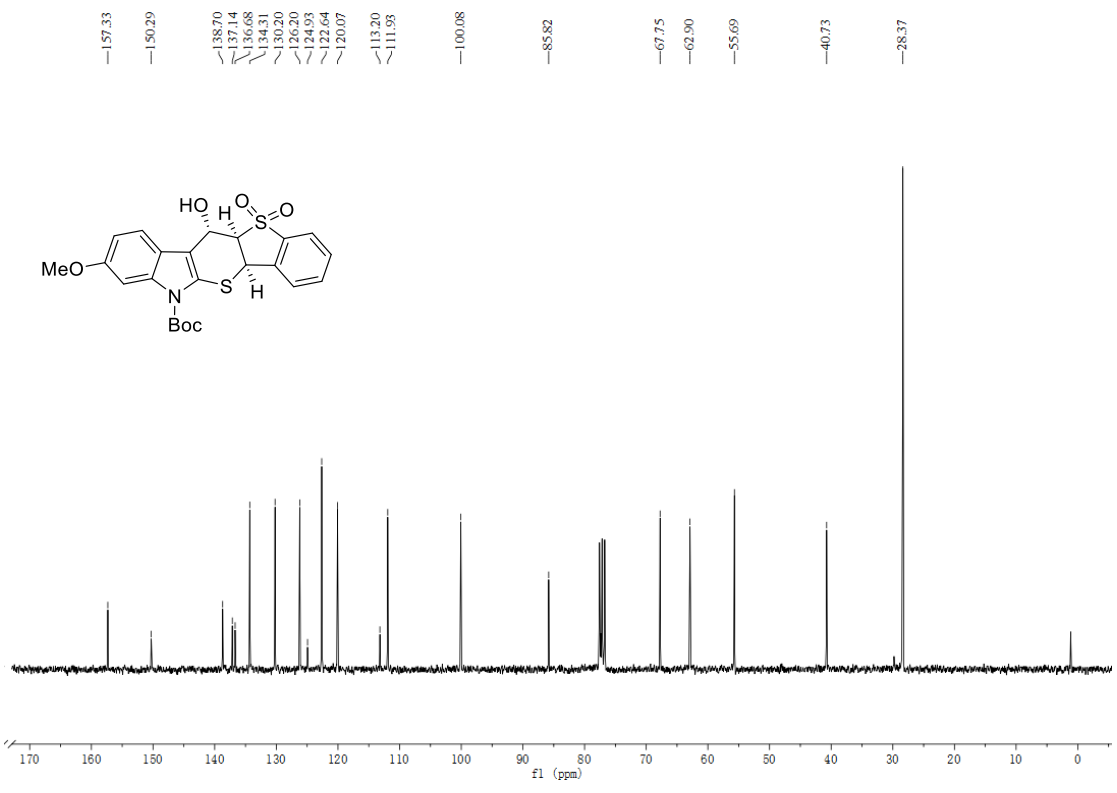


Detector A Ch1 254nm

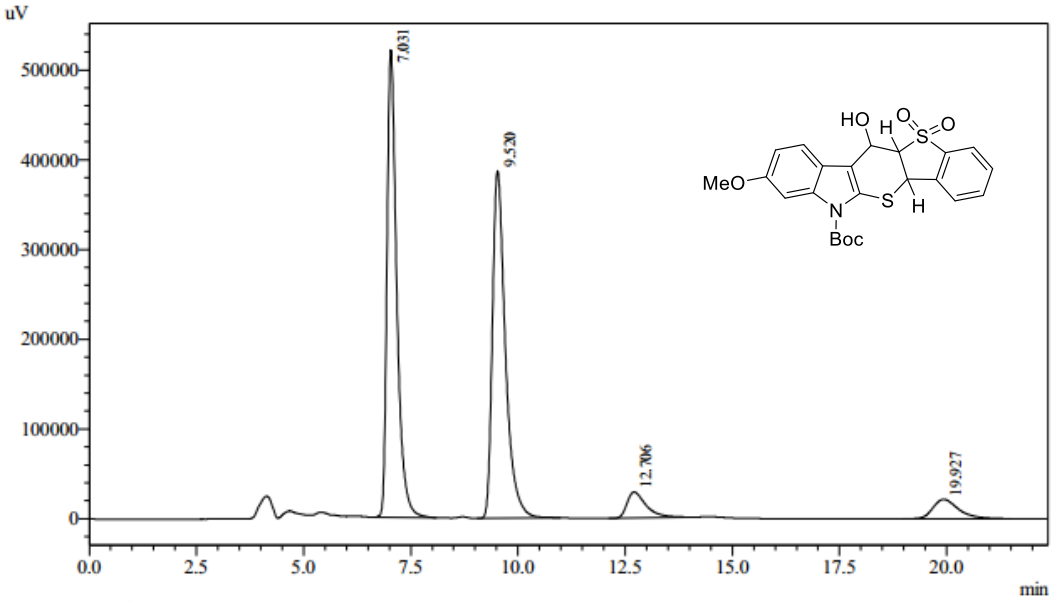
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.166	98450	6845	1.434	2.338
2	9.990	6583183	280154	95.912	95.690
3	12.345	145269	4869	2.116	1.663
4	22.199	36882	905	0.537	0.309
Total		6863784	292773	100.000	100.000

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





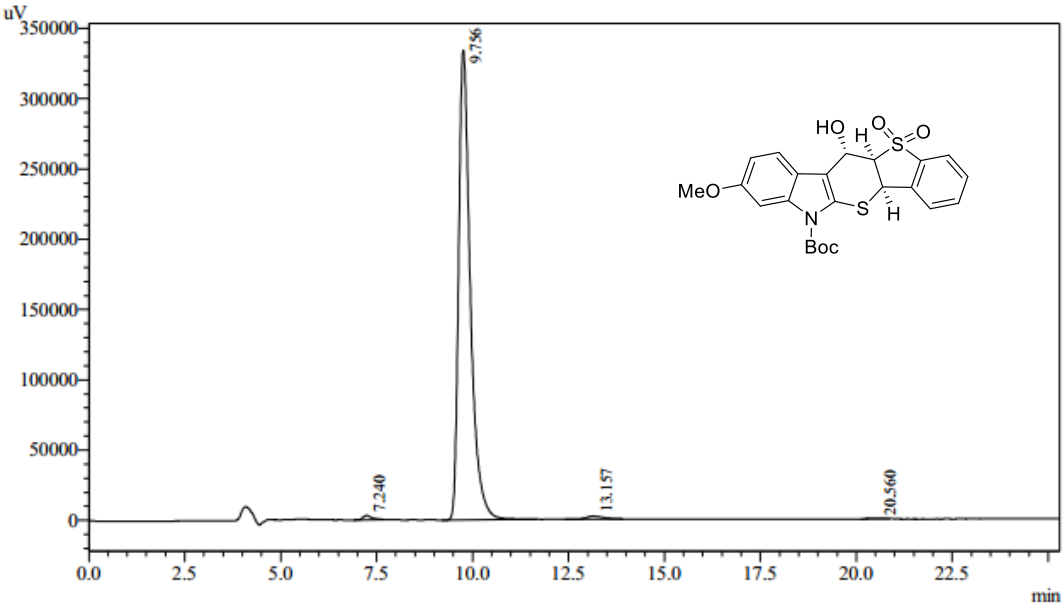
HPLC of **3i**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.031	8216537	520947	45.275	54.337
2	9.520	8144136	387236	44.876	40.390
3	12.706	885617	28869	4.880	3.011
4	19.927	901732	21683	4.969	2.262
Total		18148022	958735	100.000	100.000

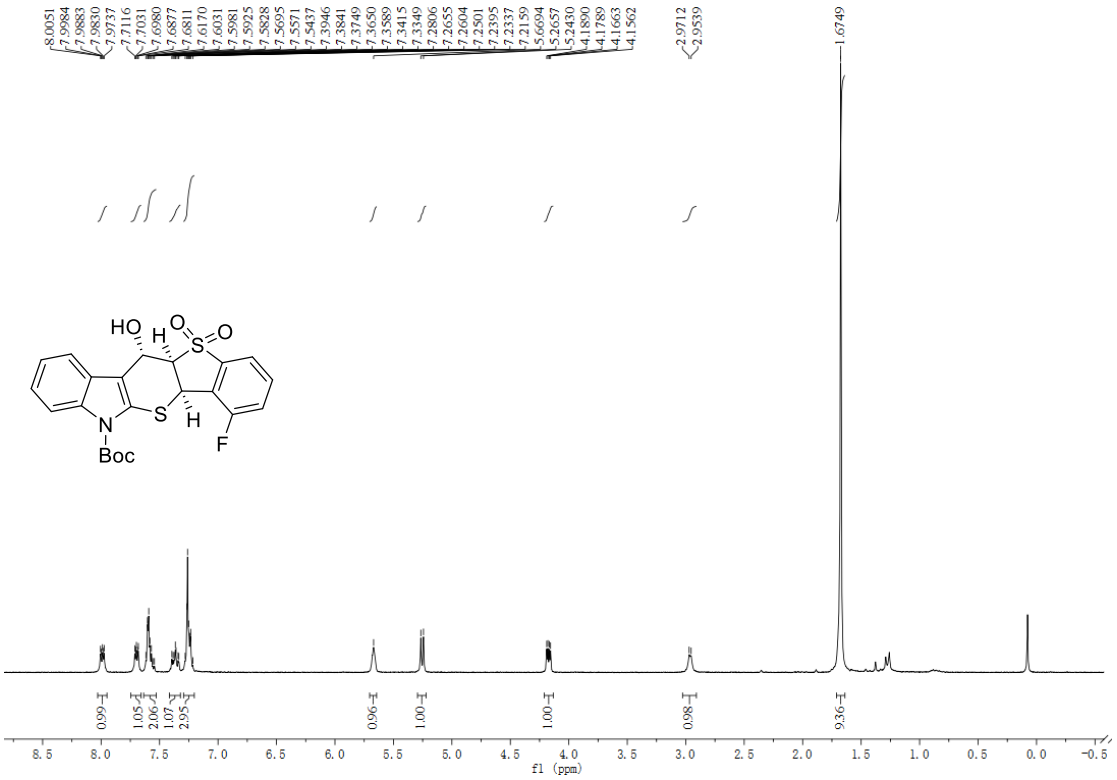


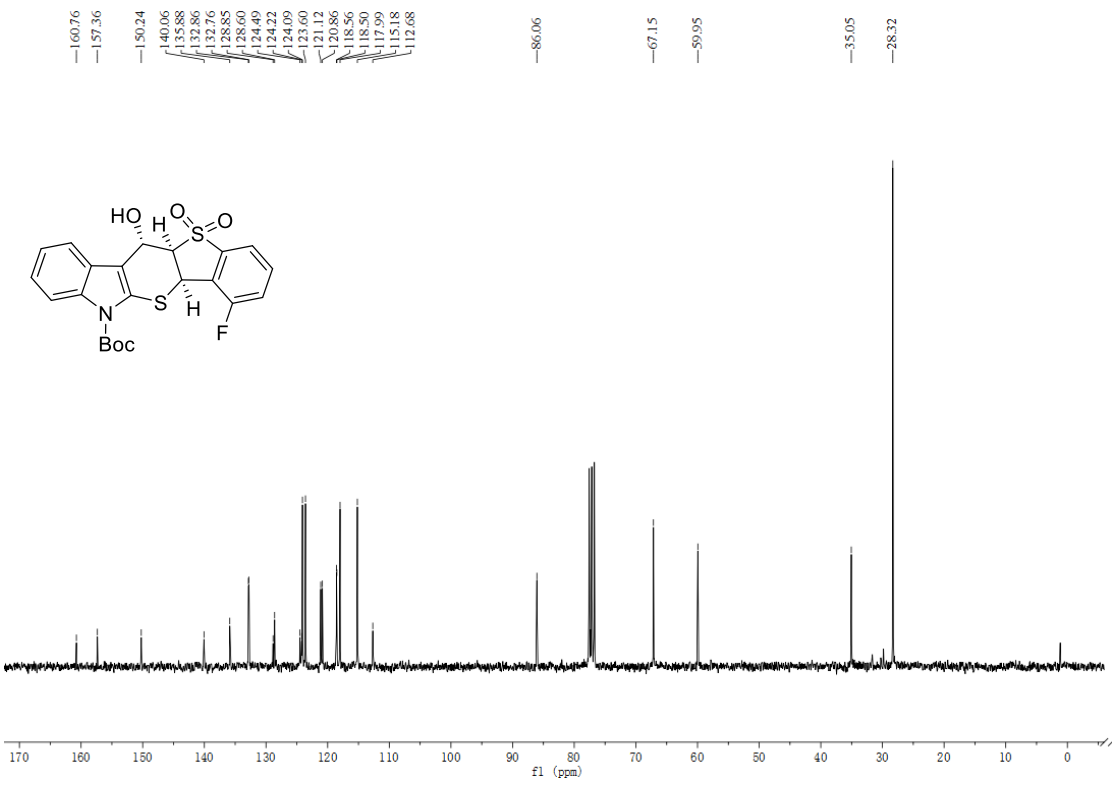
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

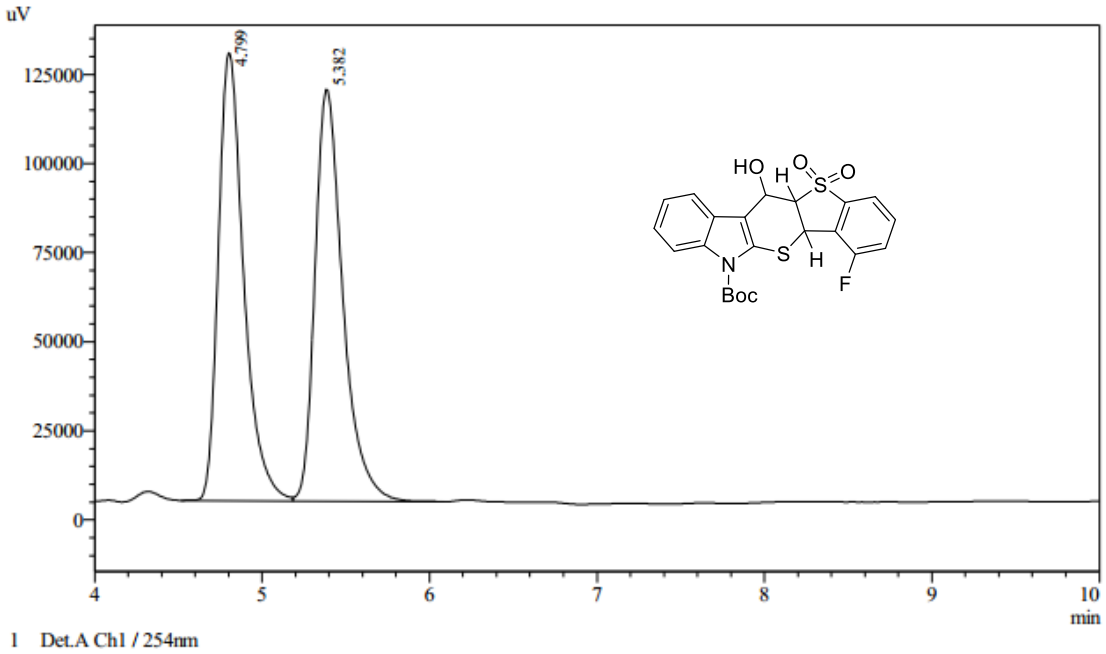
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.240	49220	3040	0.682	0.895
2	9.756	7107841	334418	98.418	98.458
3	13.157	63915	2107	0.885	0.620
4	20.560	1112	89	0.015	0.026
Total		7222087	339654	100.000	100.000

^{1}H and ^{13}C NMR of **3j**





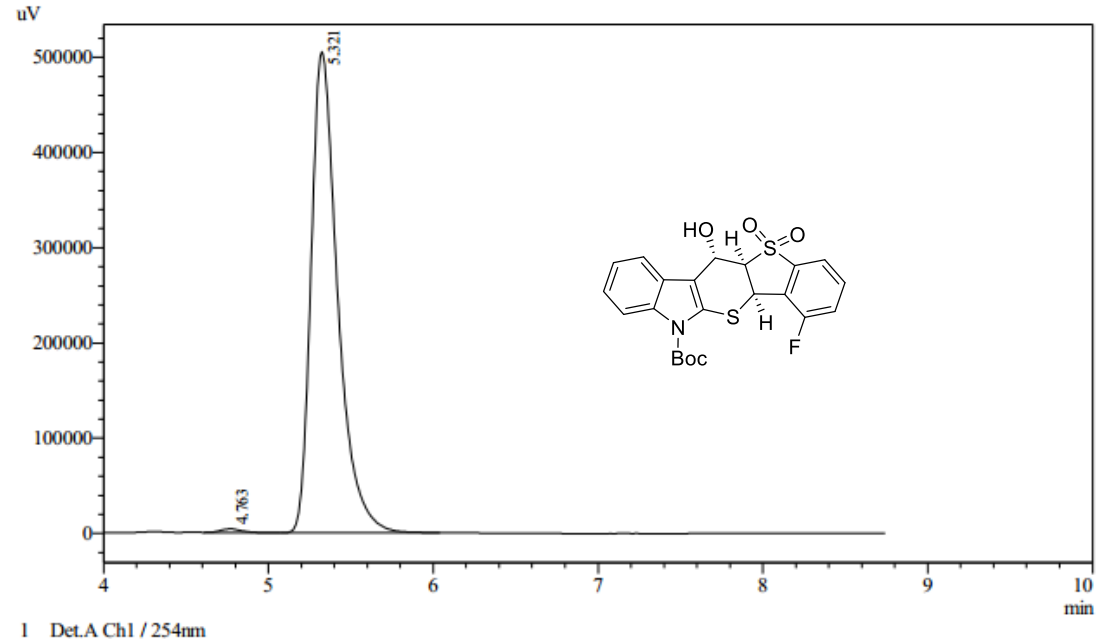
HPLC of **3j**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.799	1325077	125718	49.797	52.108
2	5.382	1335859	115548	50.203	47.892
Total		2660936	241266	100.000	100.000

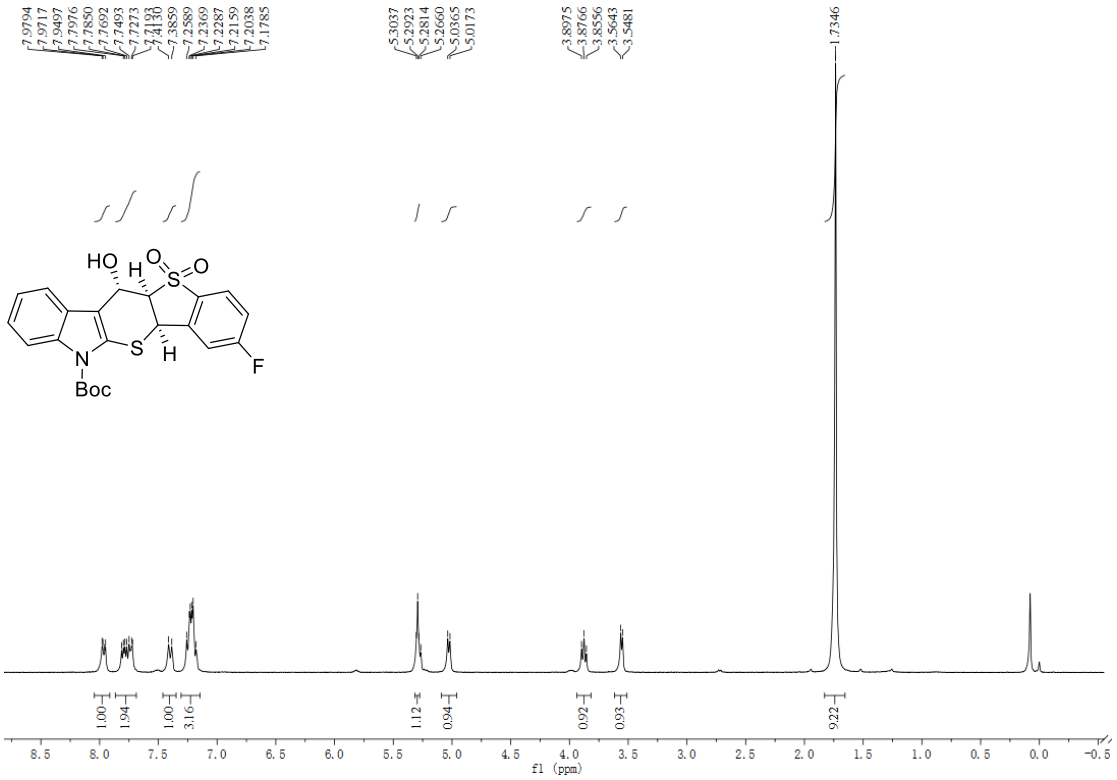


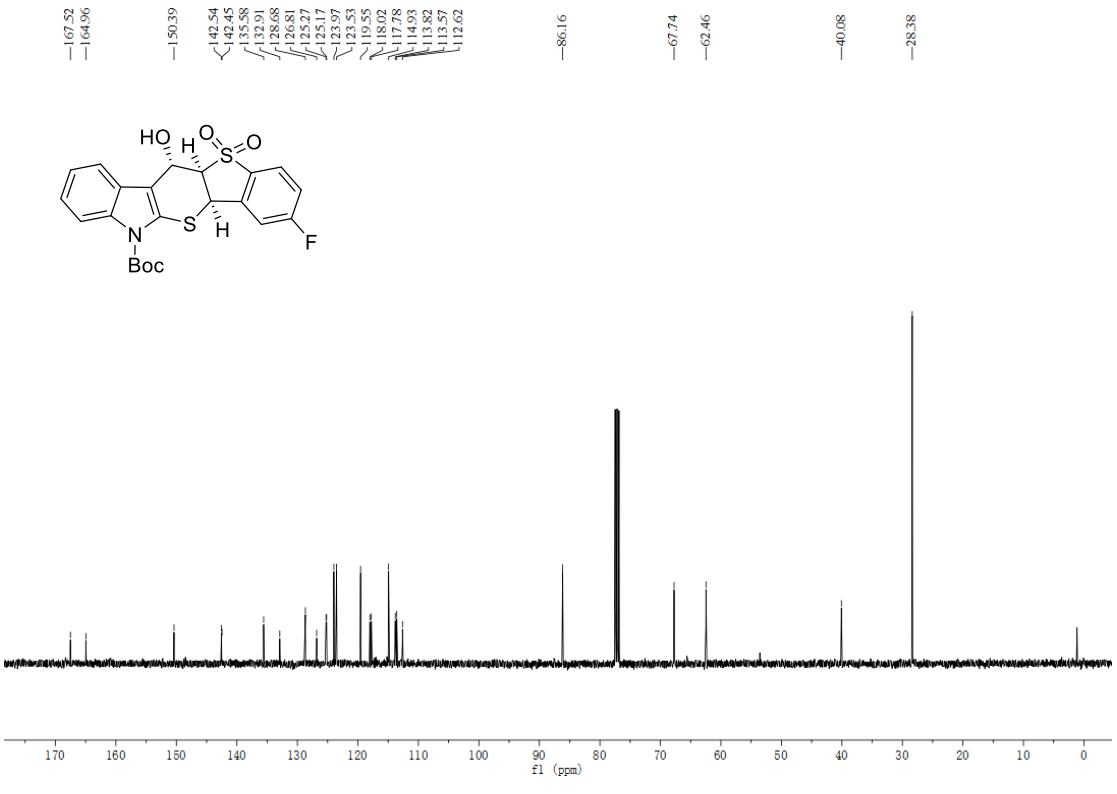
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

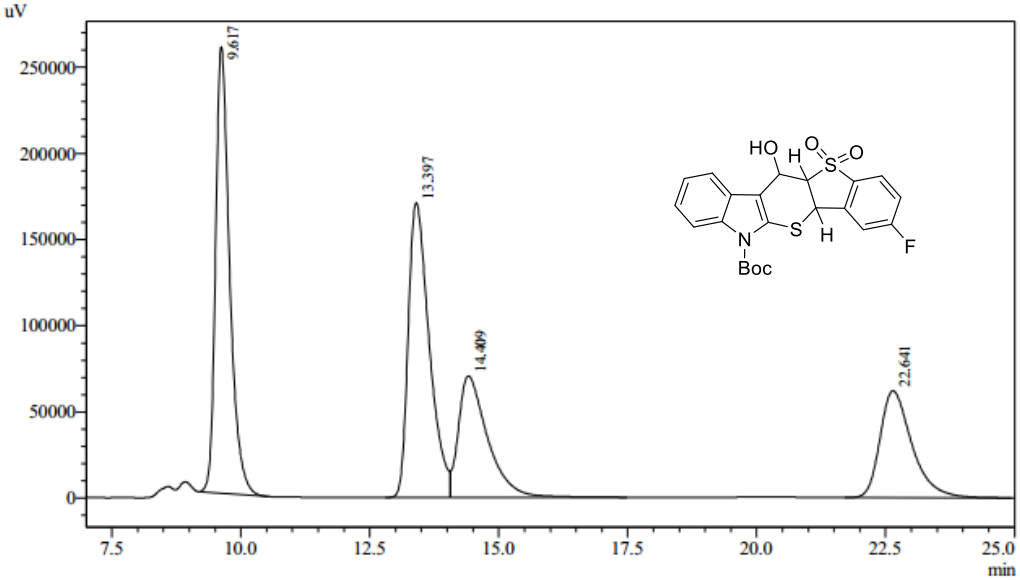
Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.763	34684	3803	0.606	0.747
2	5.321	5685126	505307	99.394	99.253
Total		5719811	509110	100.000	100.000

^{1}H and ^{13}C NMR of **3k**





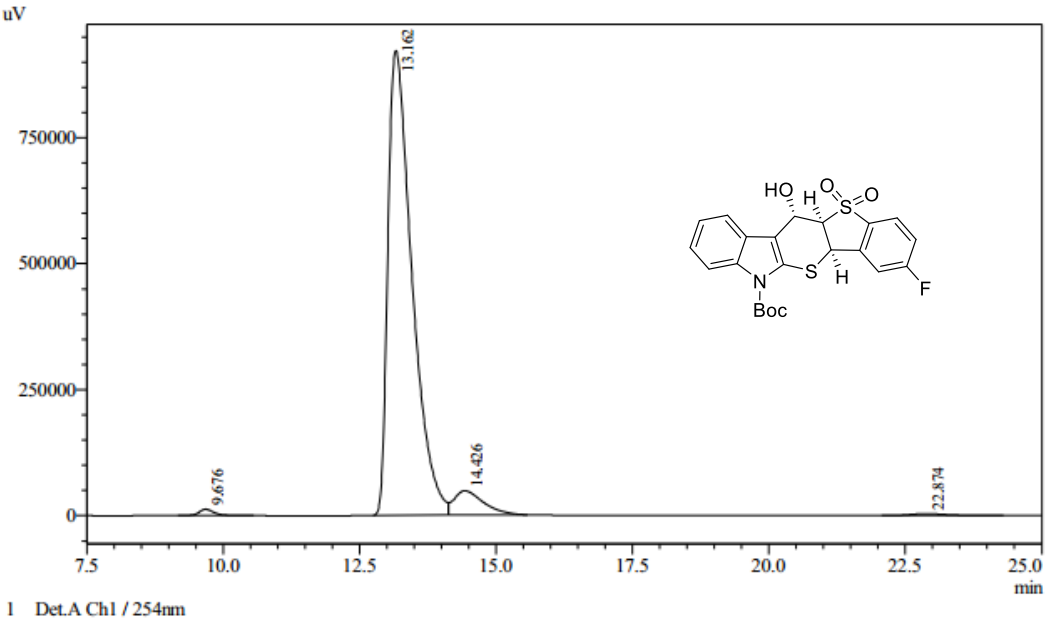
HPLC of **3k**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.617	4923019	259090	32.369	46.067
2	13.397	4846001	170959	31.863	30.397
3	14.409	2771492	70406	18.223	12.518
4	22.641	2668359	61969	17.545	11.018
Total		15208871	562424	100.000	100.000

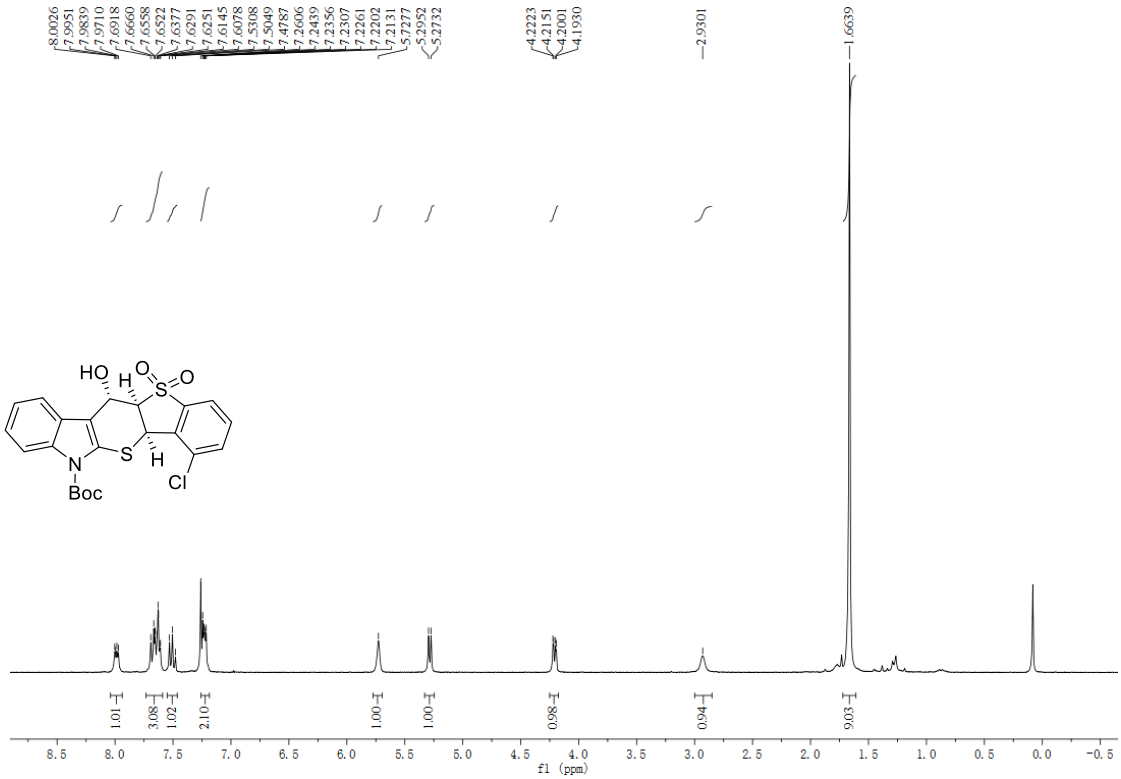


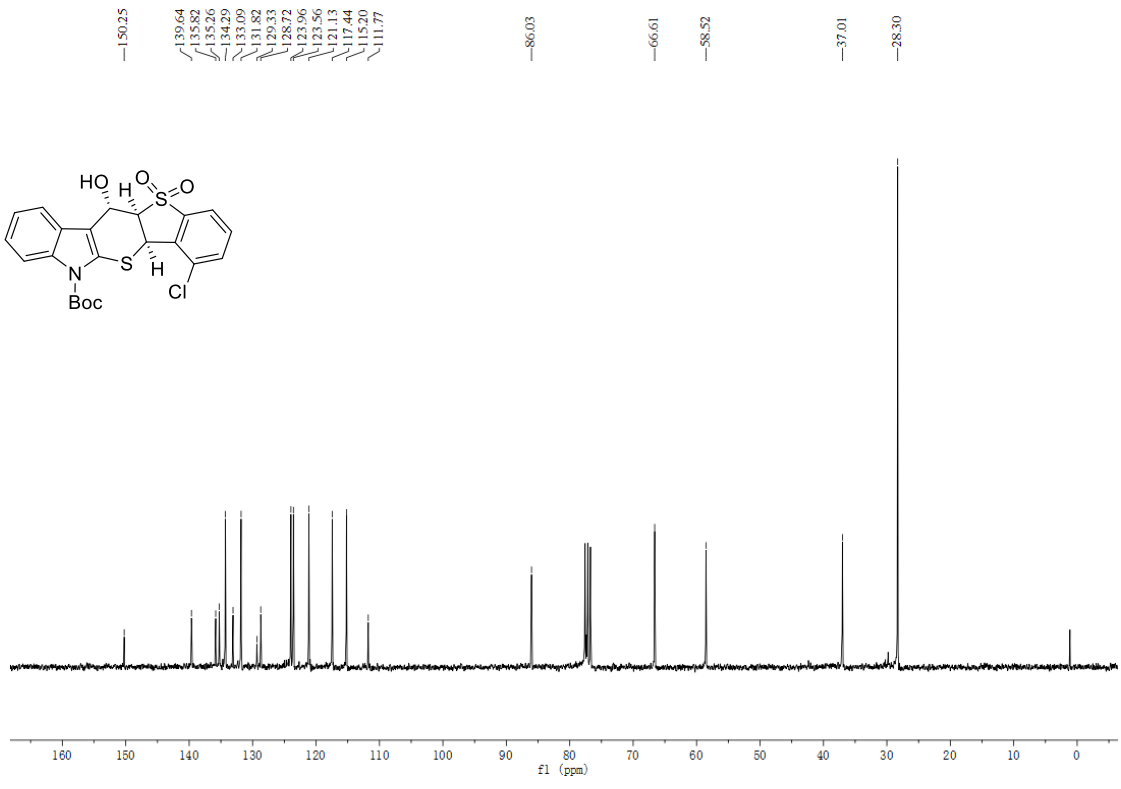
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

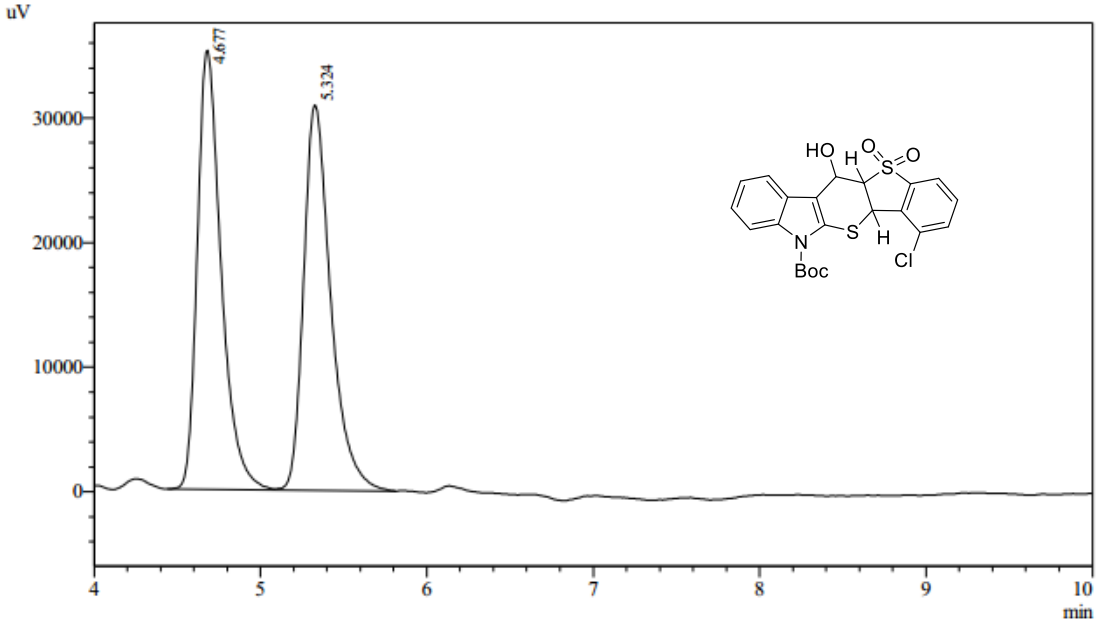
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.676	246014	12643	0.806	1.281
2	13.162	28273348	922276	92.623	93.434
3	14.426	1834654	48331	6.010	4.896
4	22.874	171292	3840	0.561	0.389
Total		30525307	987091	100.000	100.000

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





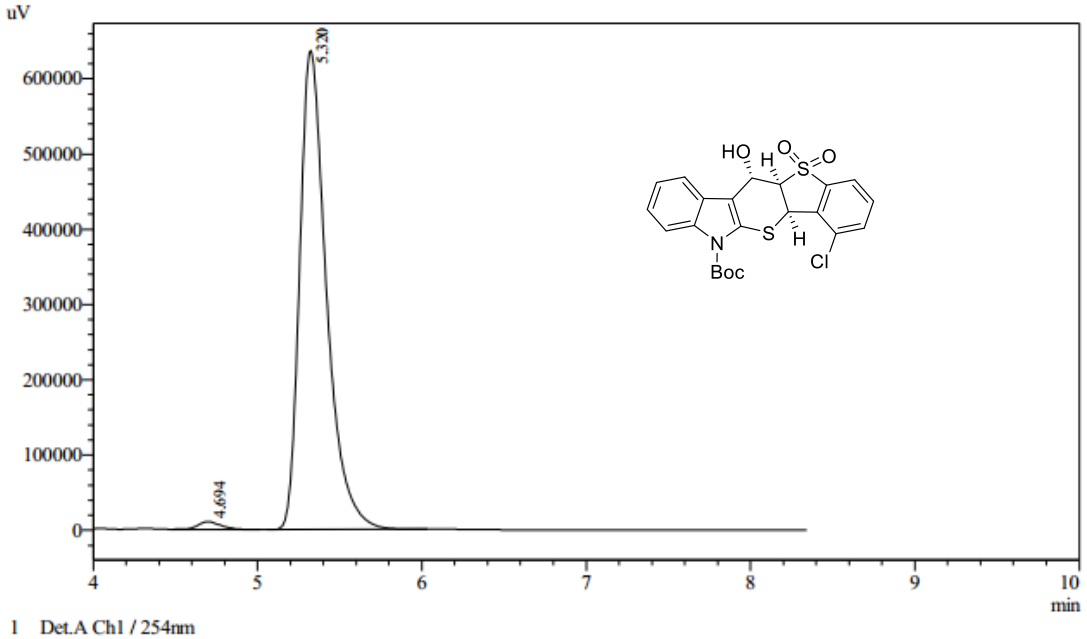
HPLC of **3l**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.677	352139	35219	50.065	53.282
2	5.324	351226	30880	49.935	46.718
Total		703364	66100	100.000	100.000

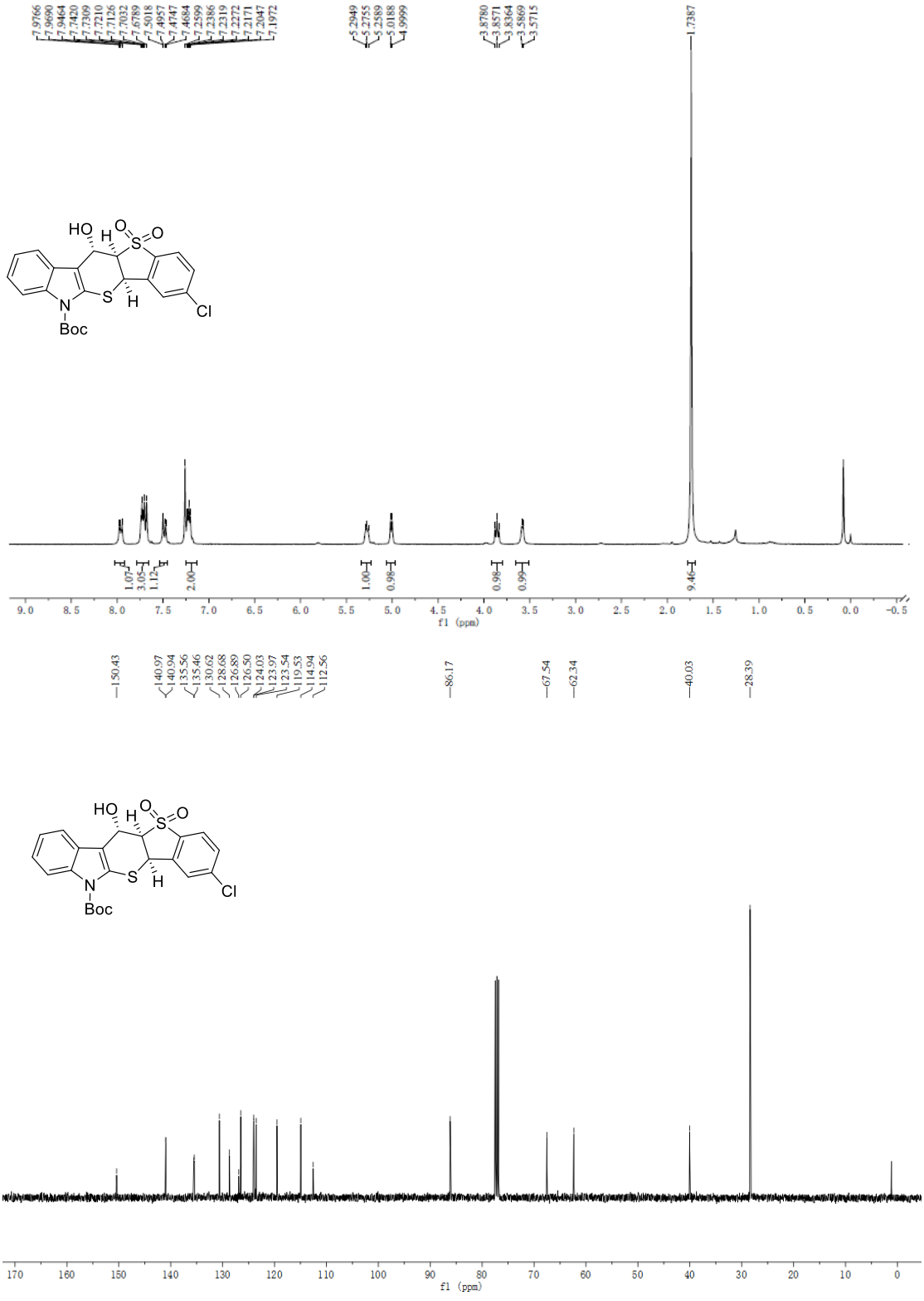


1 Det.A Ch1 / 254nm

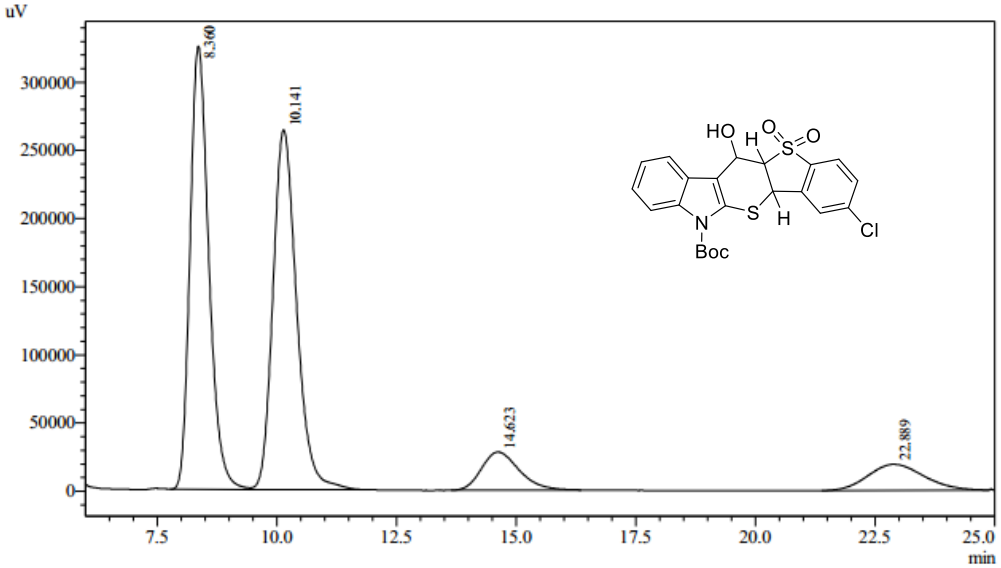
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.694	98879	10243	1.351	1.583
2	5.320	7219896	636679	98.649	98.417
Total		7318775	646923	100.000	100.000

^{1}H and ^{13}C NMR of **3m**



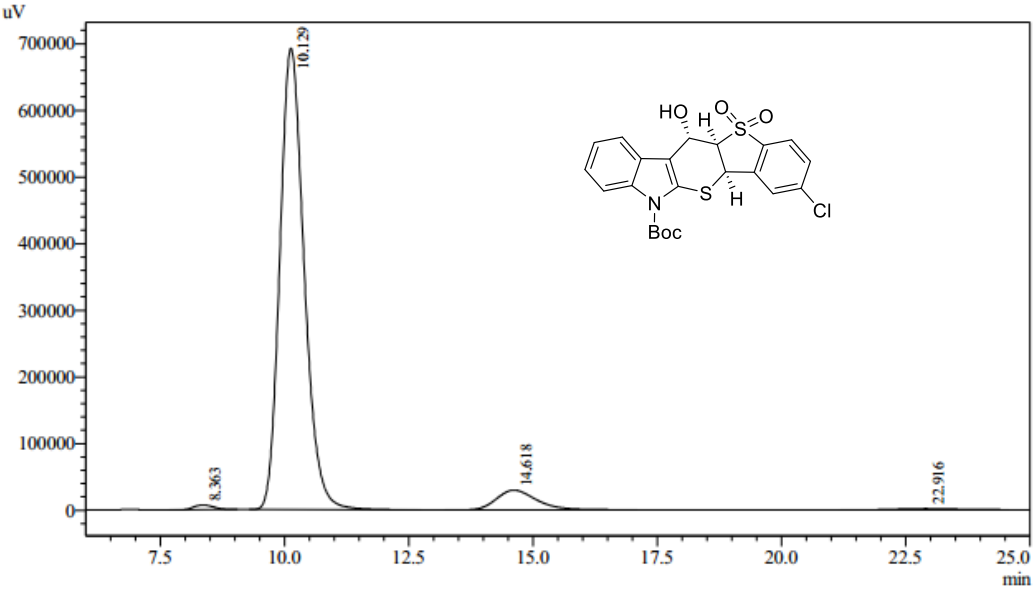
HPLC of **3m**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.360	8866221	324945	42.169	51.104
2	10.141	9055227	263761	43.067	41.481
3	14.623	1542392	27994	7.336	4.403
4	22.889	1561832	19157	7.428	3.013
Total		21025672	635856	100.000	100.000

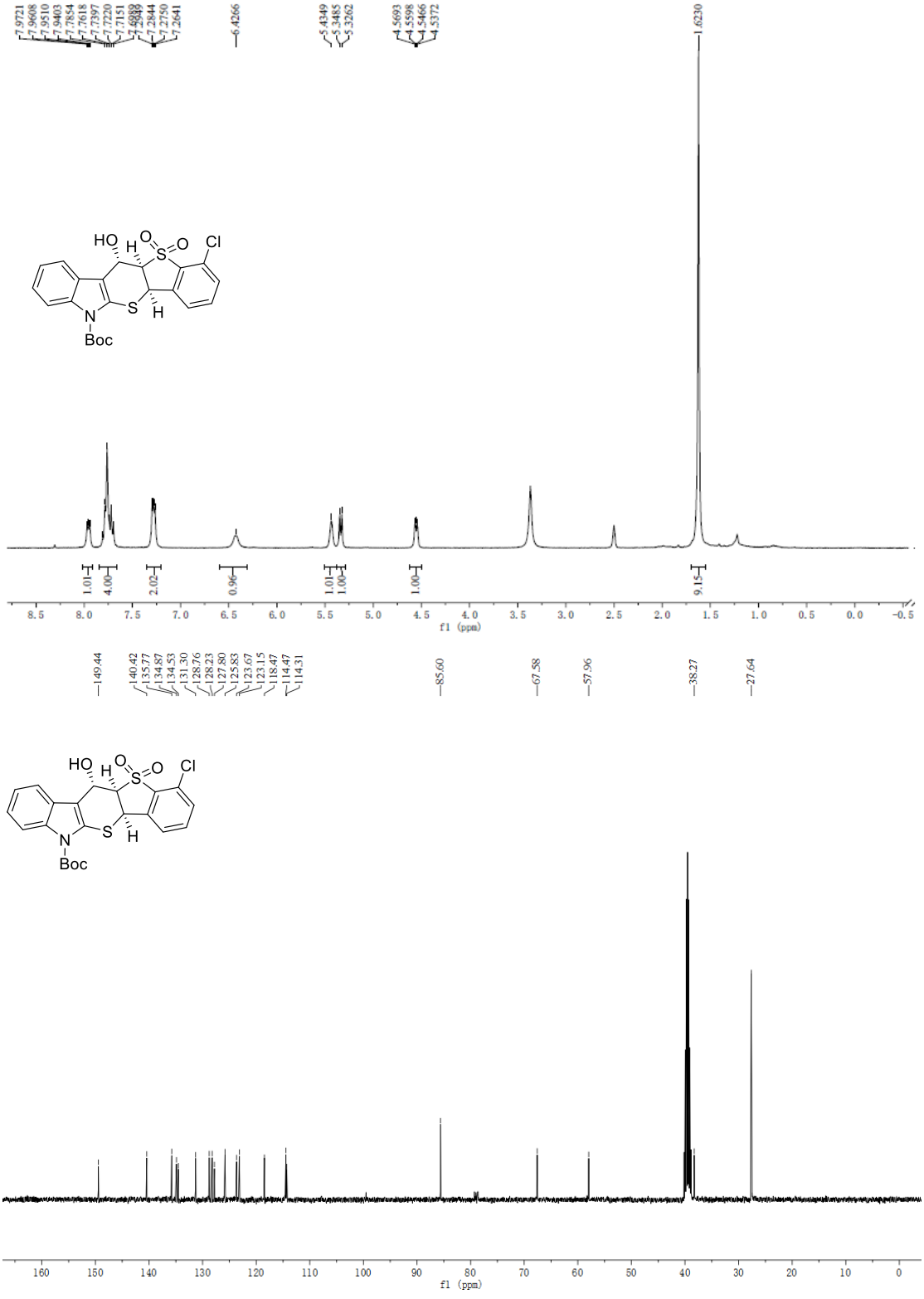


1 Det.A Ch1 / 254nm

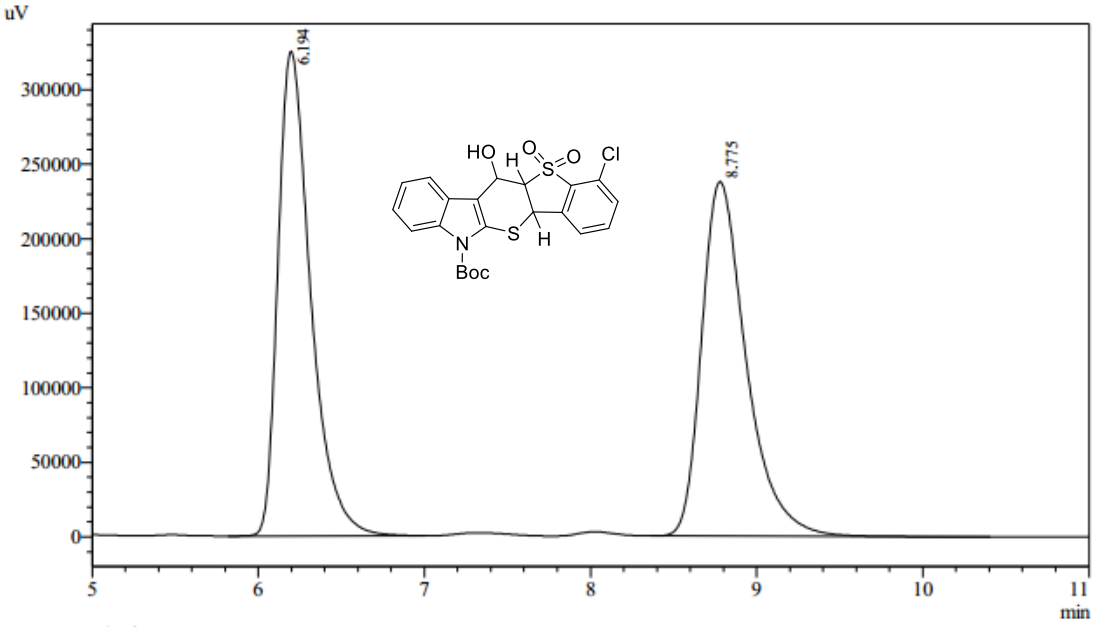
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.363	188915	6946	0.739	0.951
2	10.129	23546523	692367	92.170	94.756
3	14.618	1674902	29618	6.556	4.053
4	22.916	136591	1754	0.535	0.240
Total		25546930	730684	100.000	100.000

^{1}H and ^{13}C NMR of **3n**



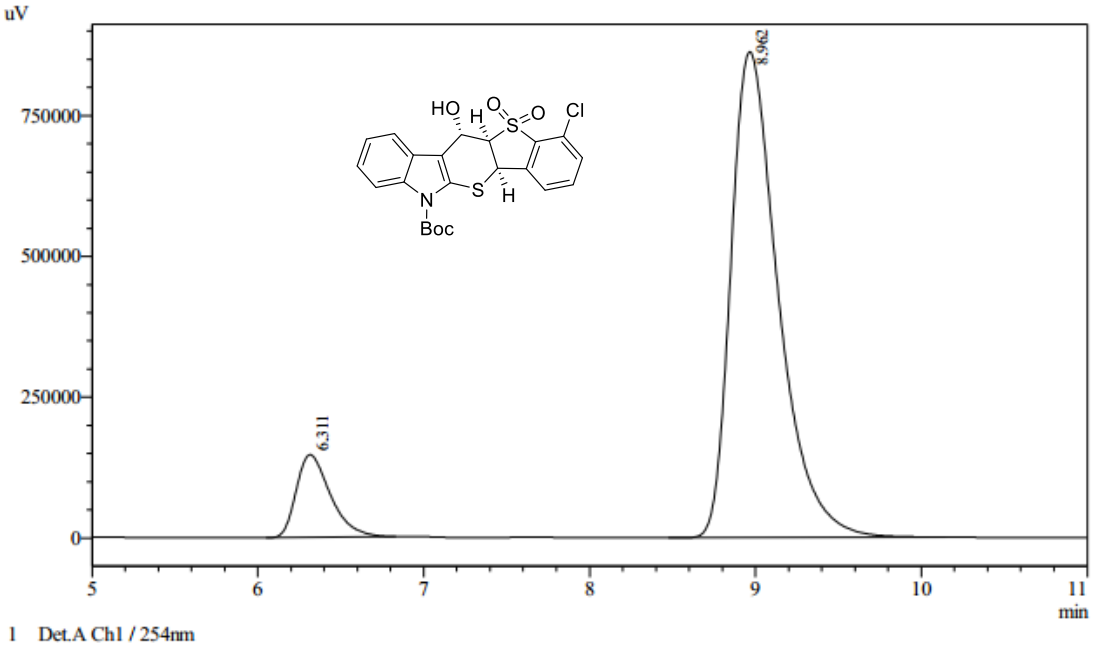
HPLC of **3n**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.194	4458044	325310	50.081	57.765
2	8.775	4443547	237854	49.919	42.235
Total		8901591	563164	100.000	100.000

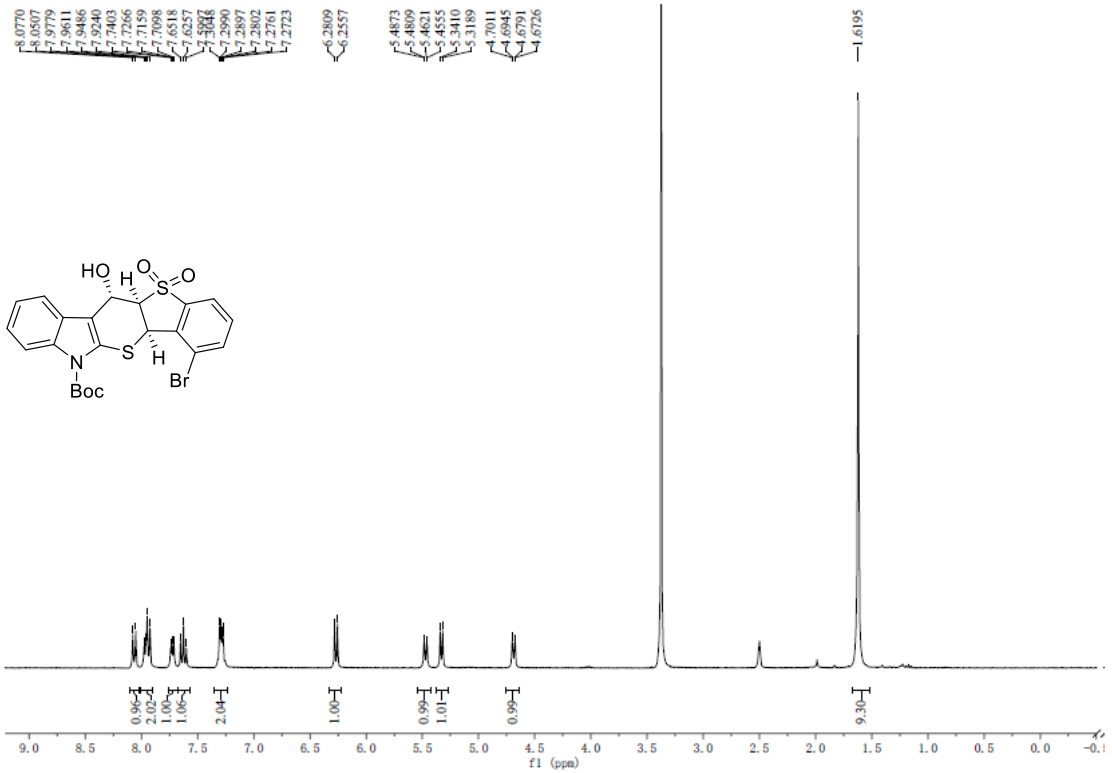


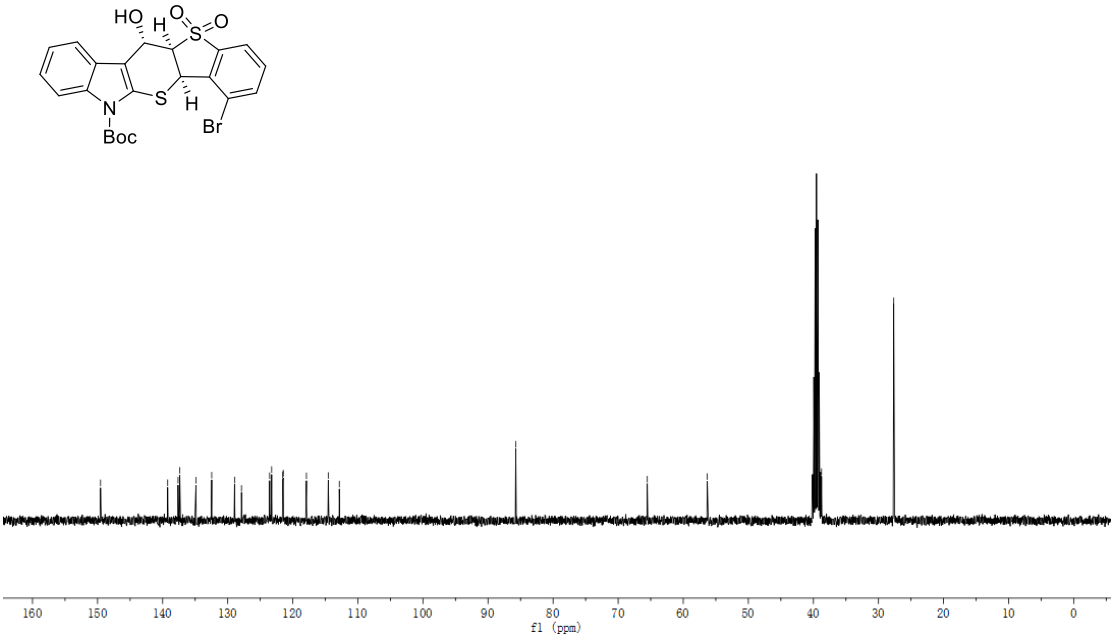
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

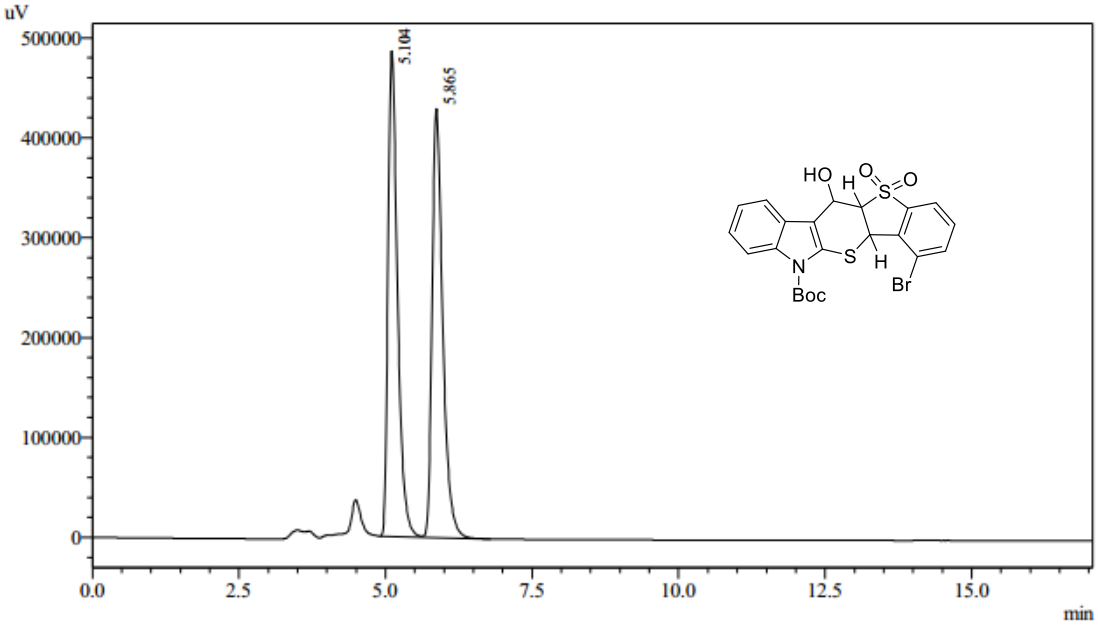
Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.311	2110071	146741	10.965	14.531
2	8.962	17133517	863099	89.035	85.469
Total		19243588	1009840	100.000	100.000

^{1}H and ^{13}C NMR of **3o**





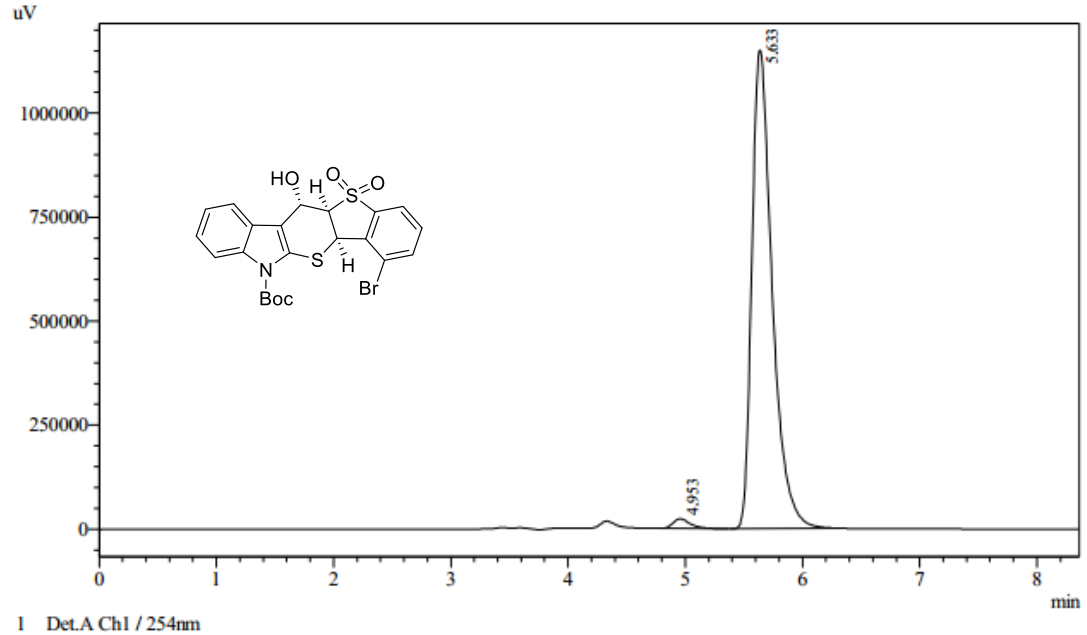
HPLC of **3o**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.104	5460255	486077	50.173	53.094
2	5.865	5422614	429427	49.827	46.906
Total		10882869	915504	100.000	100.000

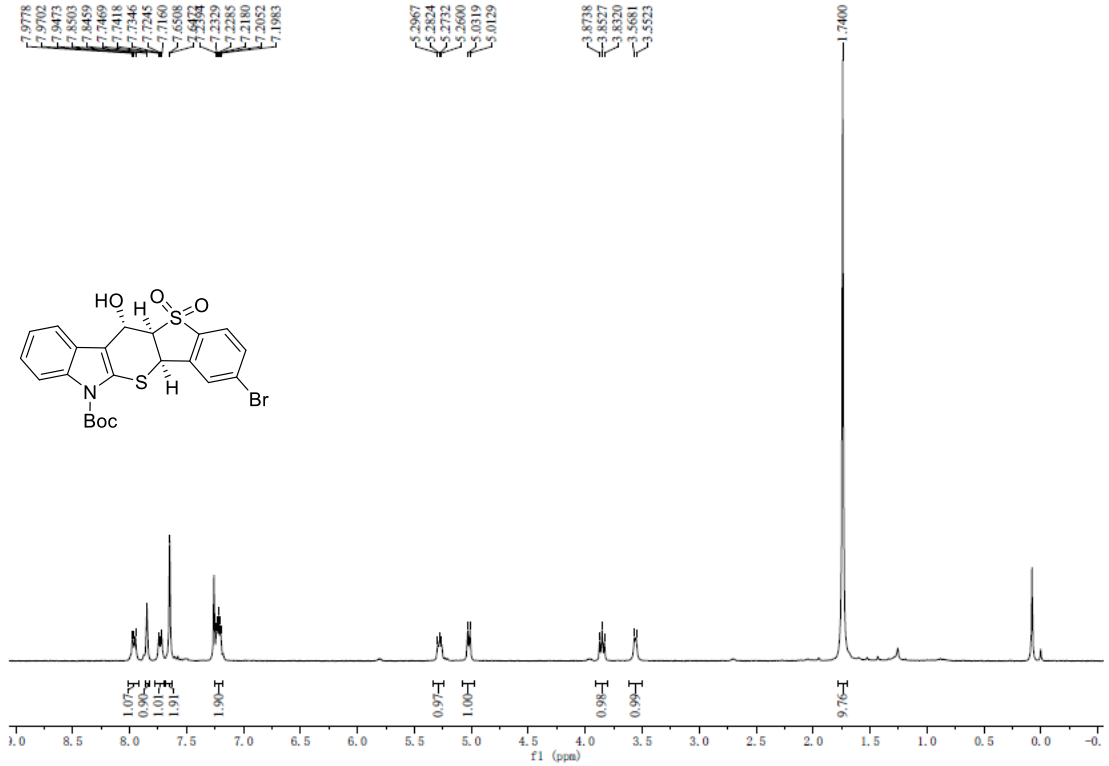


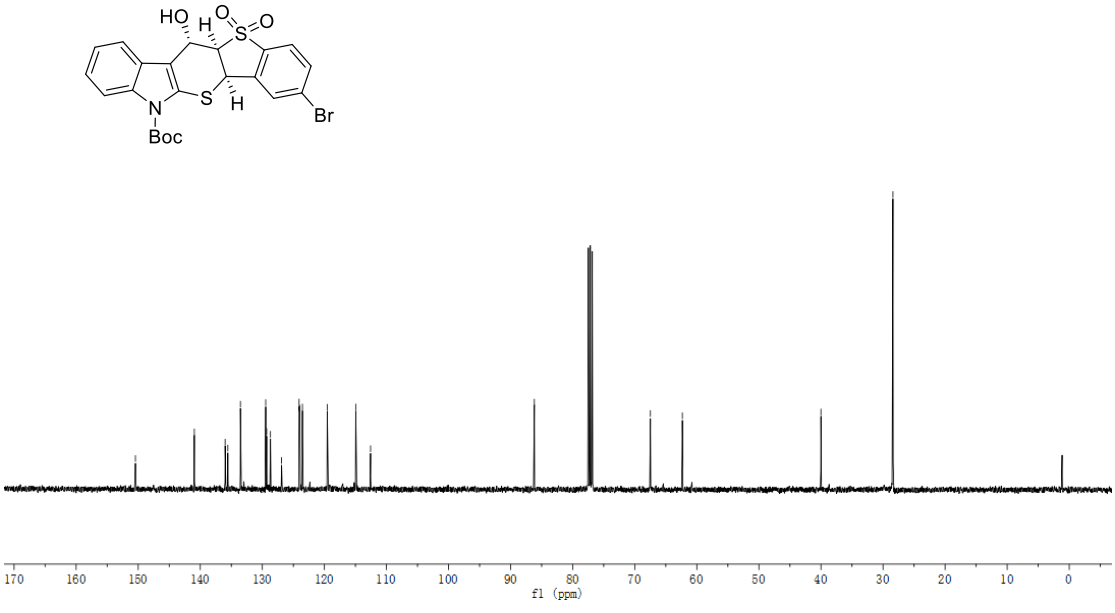
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

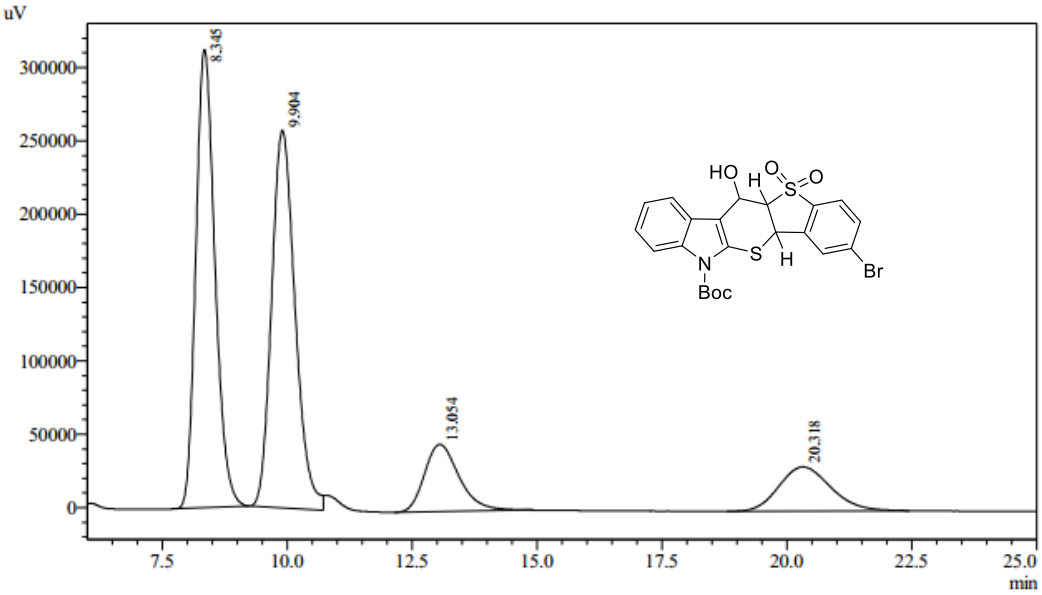
Peak#	Ret. Time	Area	Height	Area %	Height %
1	4.953	238799	23071	1.691	1.967
2	5.633	13879209	1149661	98.309	98.033
Total		14118008	1172732	100.000	100.000

^{1}H and ^{13}C NMR of **3p**





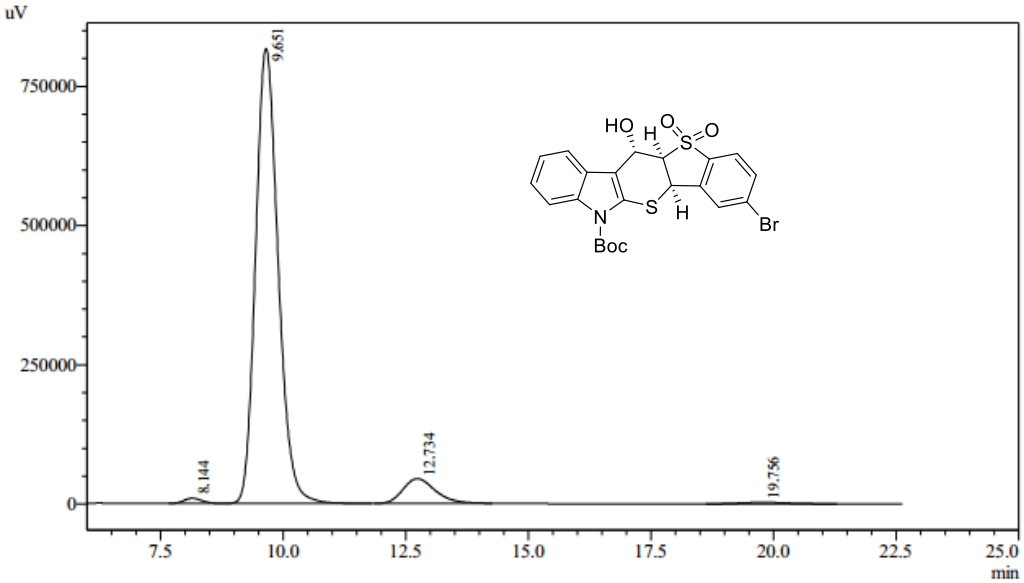
HPLC of **3p**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.345	8308634	312343	39.350	48.366
2	9.904	8406824	257426	39.815	39.862
3	13.054	2223246	45900	10.529	7.108
4	20.318	2175923	30119	10.305	4.664
Total		21114627	645788	100.000	100.000

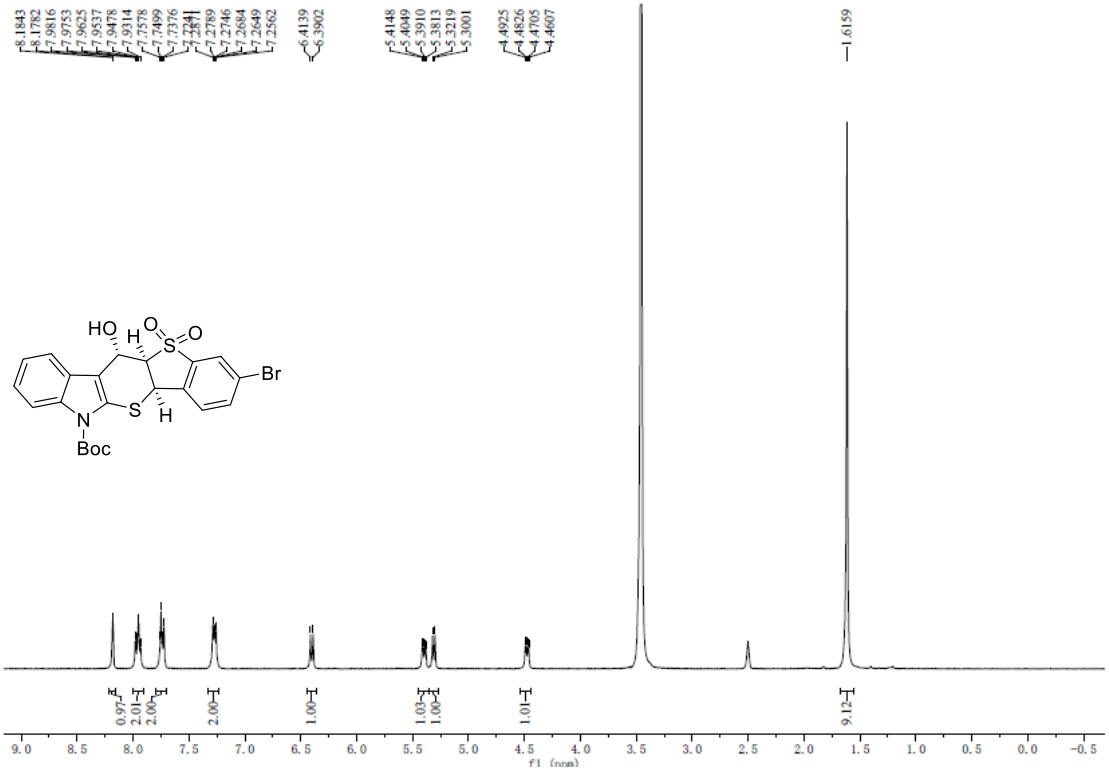


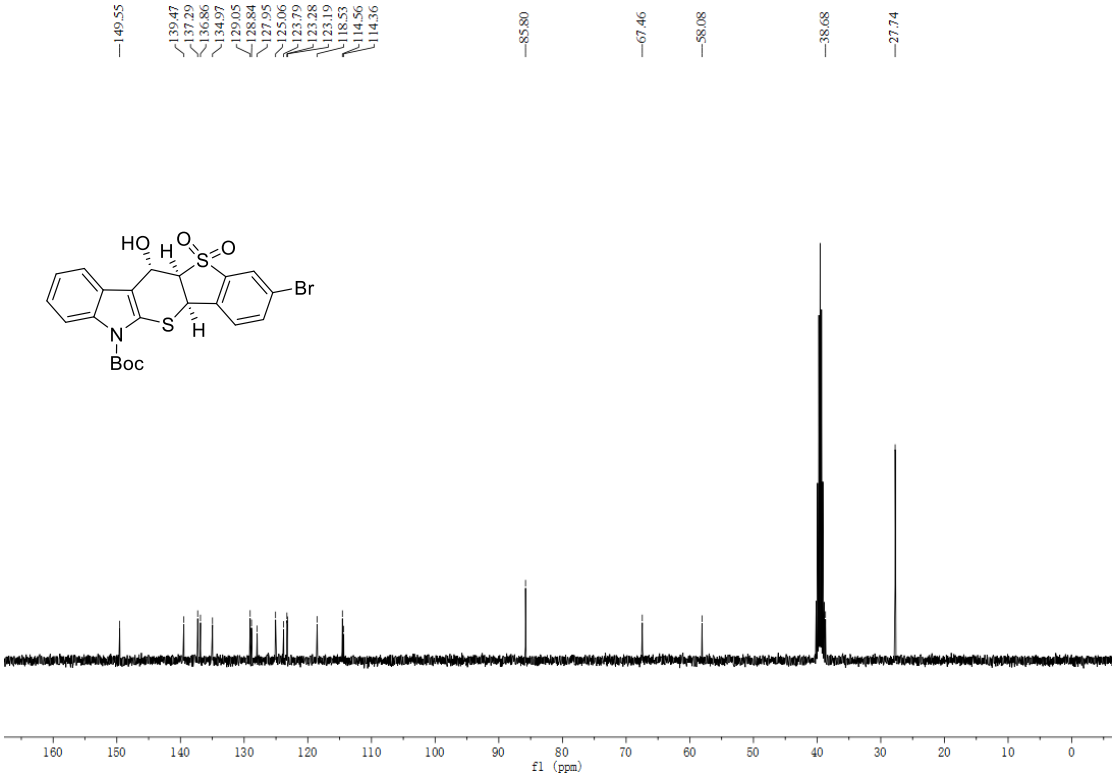
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

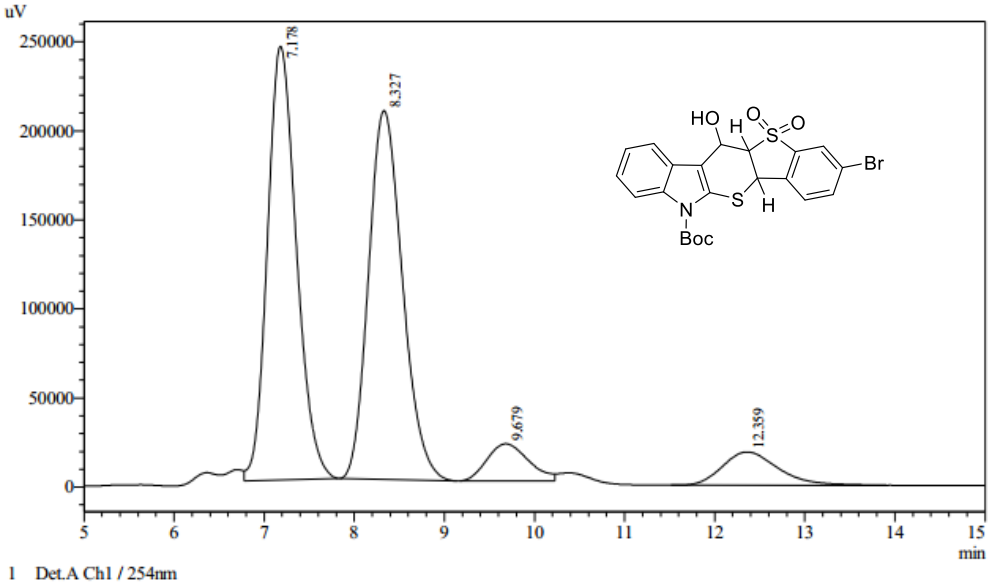
Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.144	230234	9193	0.806	1.053
2	9.651	26136261	817095	91.444	93.576
3	12.734	2043065	44366	7.148	5.081
4	19.756	172107	2537	0.602	0.291
Total		28581666	873191	100.000	100.000

^{1}H and ^{13}C NMR of **3q**





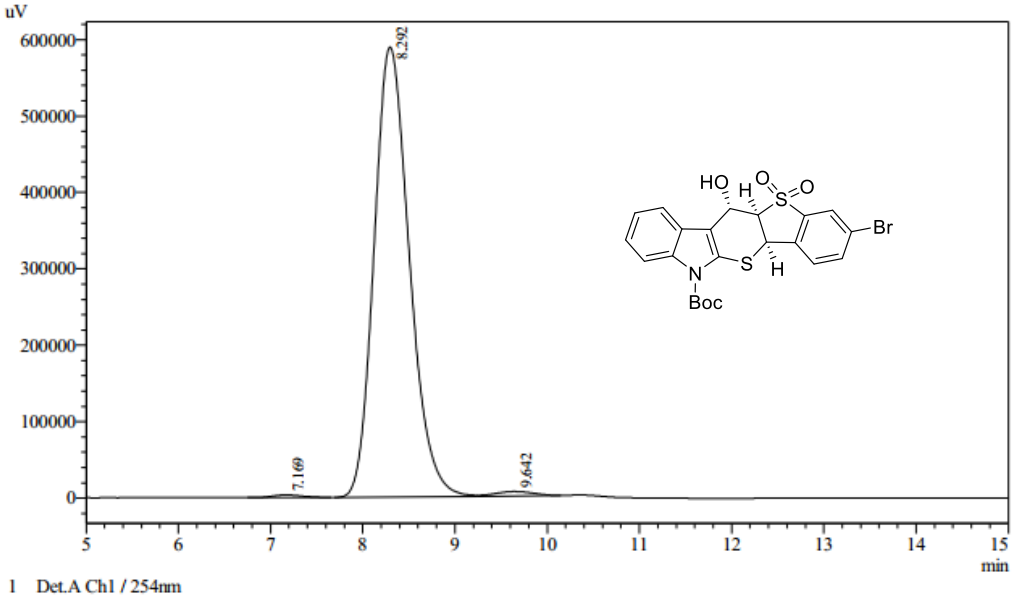
HPLC of **3q**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.178	5459430	243691	44.153	49.674
2	8.327	5424887	207259	43.873	42.248
3	9.679	676556	20959	5.472	4.272
4	12.359	804038	18668	6.503	3.805
Total		12364911	490577	100.000	100.000

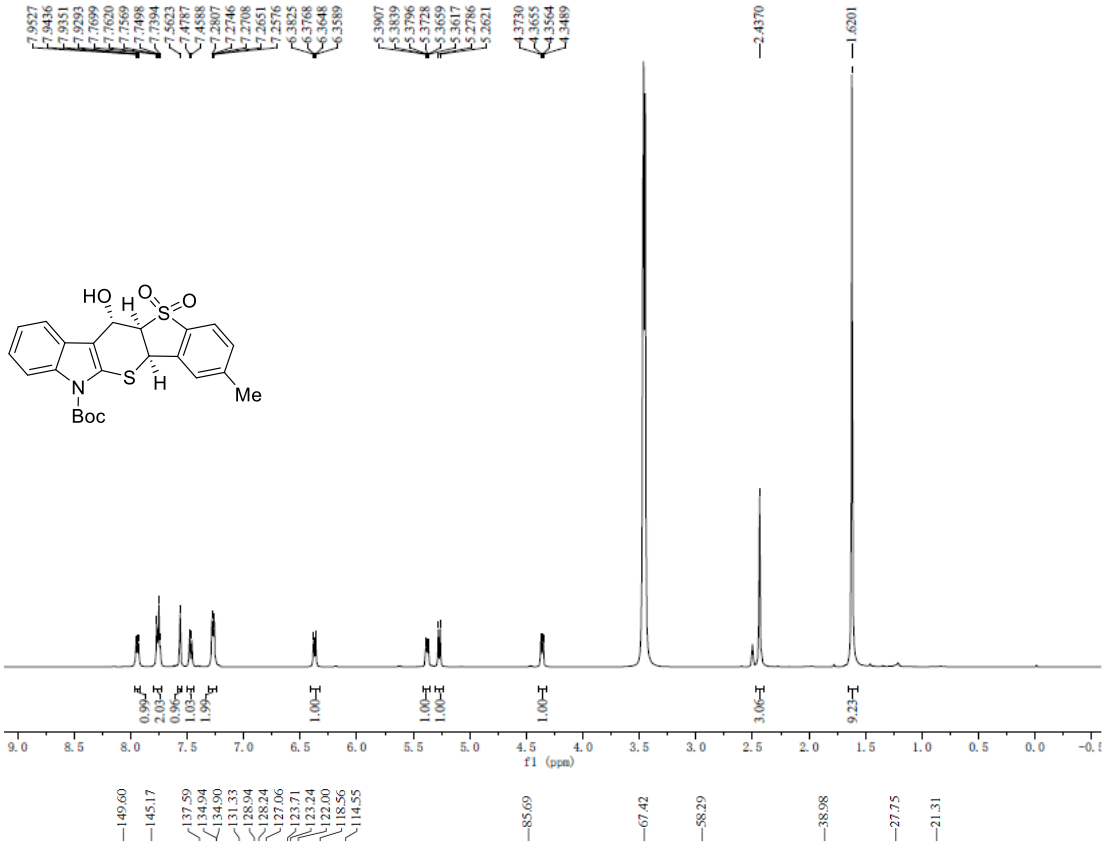


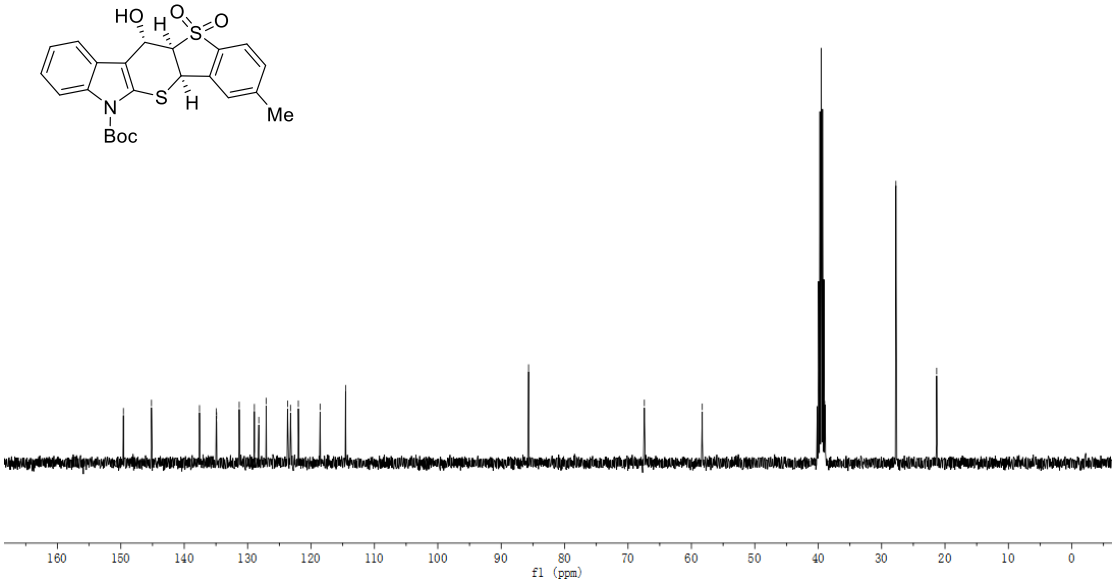
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

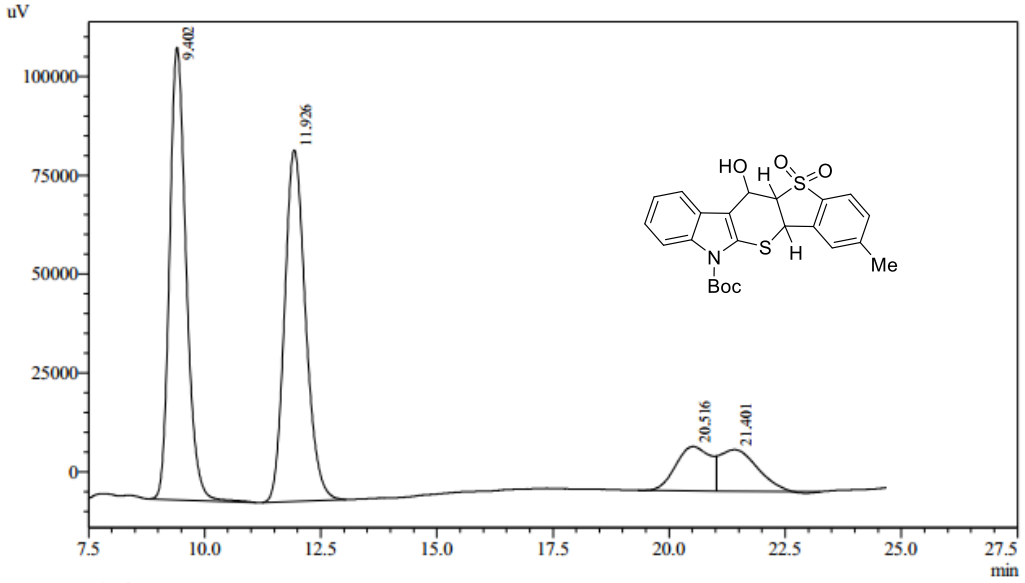
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.169	77272	3484	0.485	0.582
2	8.292	15684797	588907	98.471	98.456
3	9.642	166193	5753	1.043	0.962
Total		15928262	598144	100.000	100.000

^{1}H and ^{13}C NMR of **3r**





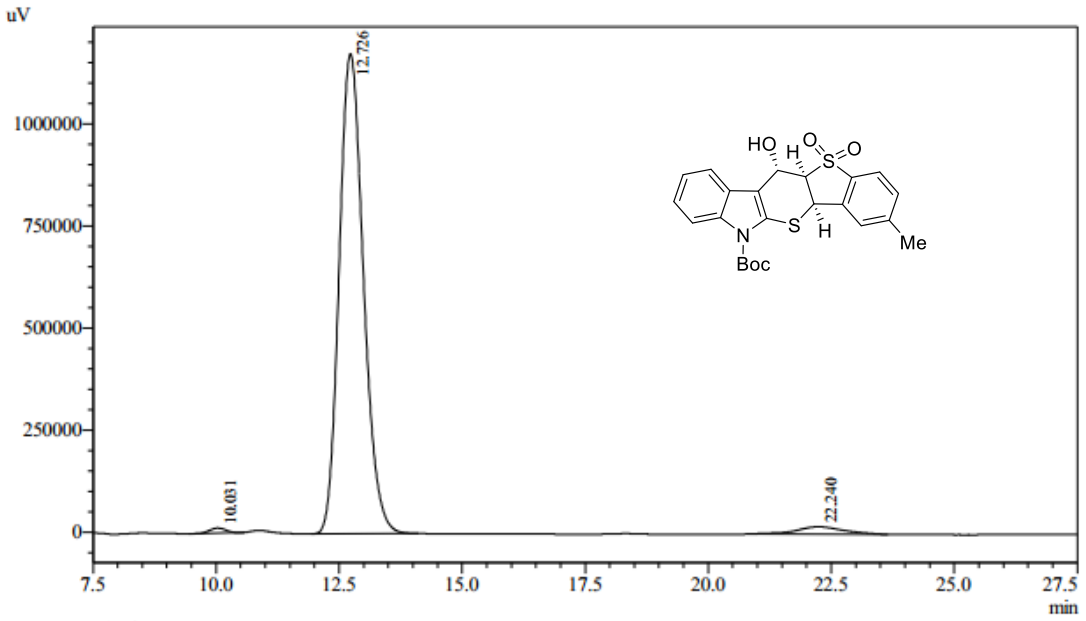
HPLC of **3r**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.402	2841963	114432	41.730	50.842
2	11.926	2798472	88943	41.091	39.517
3	20.516	589758	11193	8.660	4.973
4	21.401	580174	10507	8.519	4.668
Total		6810367	225075	100.000	100.000

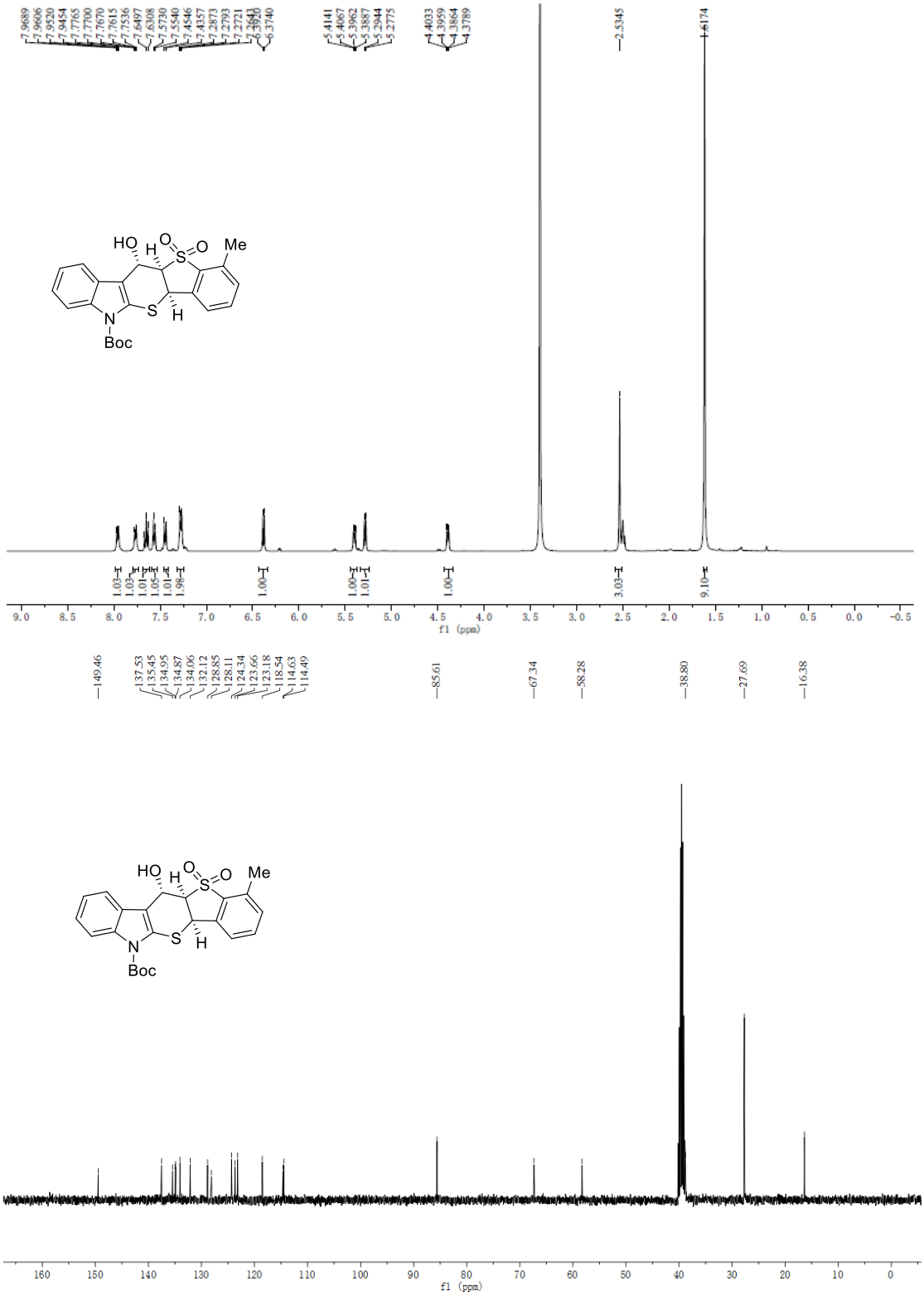


1 Det.A Ch1 / 254nm

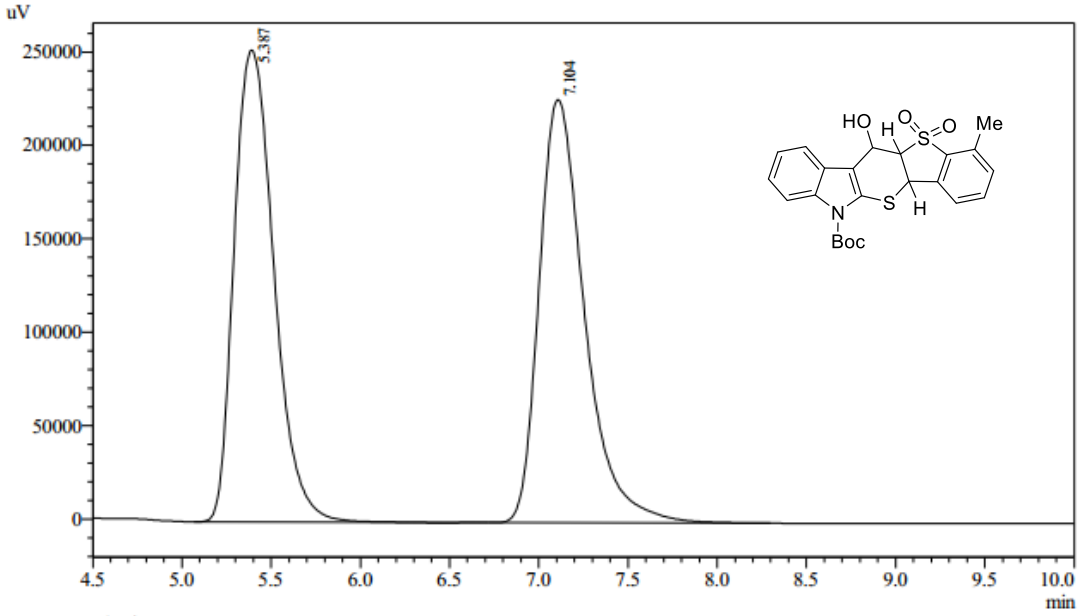
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.031	273470	12342	0.653	1.023
2	12.726	40331075	1175247	96.312	97.452
3	22.240	1270956	18382	3.035	1.524
Total		41875502	1205972	100.000	100.000

^{1}H and ^{13}C NMR of **3s**



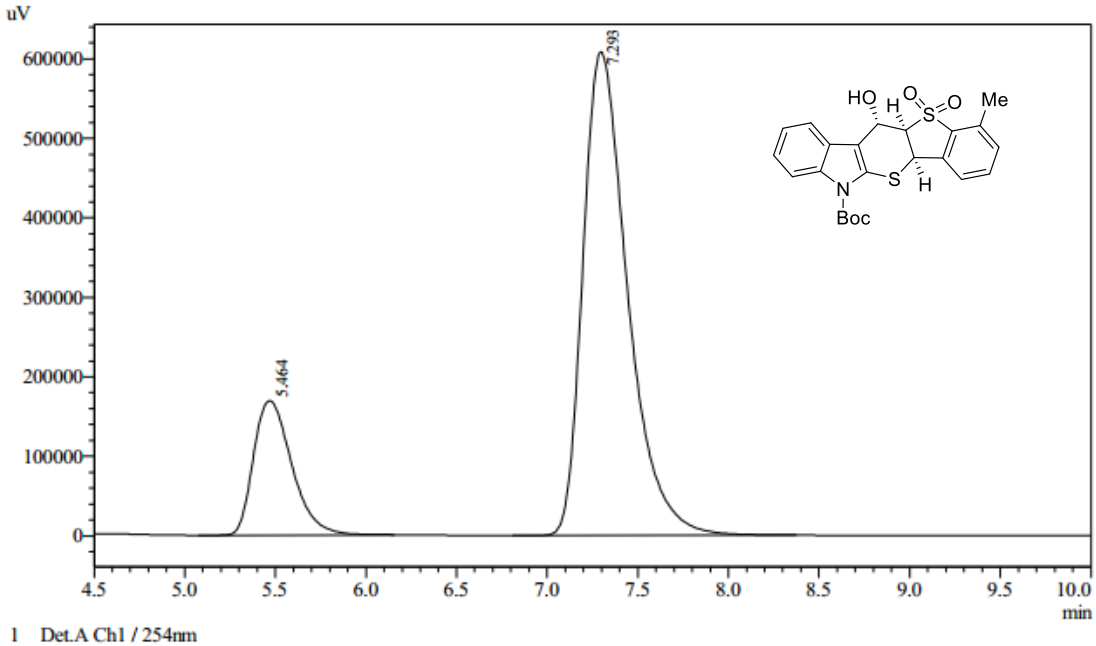
HPLC of **3s**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.387	3924728	252691	49.471	52.718
2	7.104	4008677	226634	50.529	47.282
Total		7933405	479326	100.000	100.000

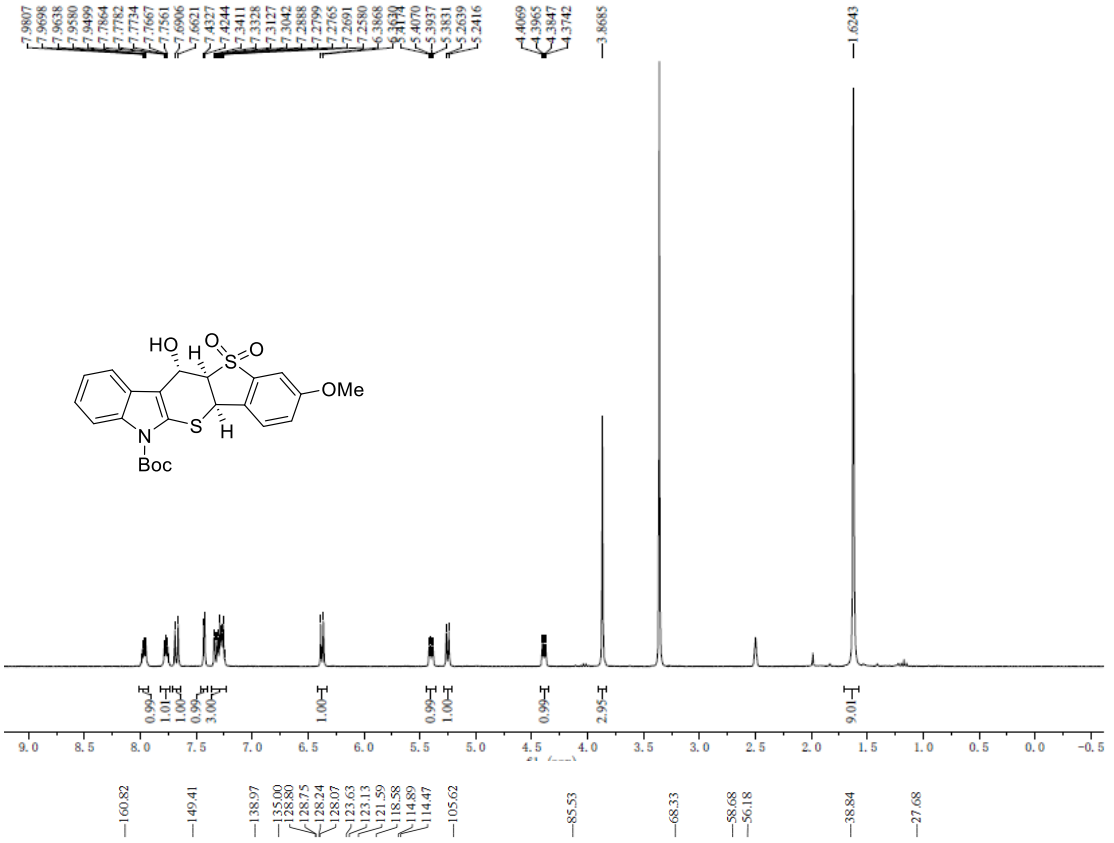


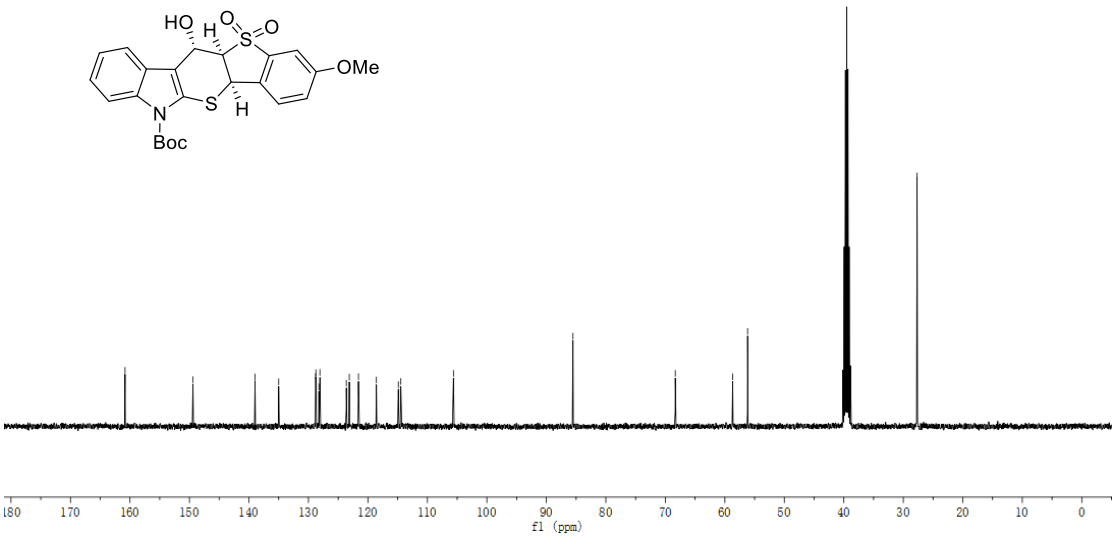
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

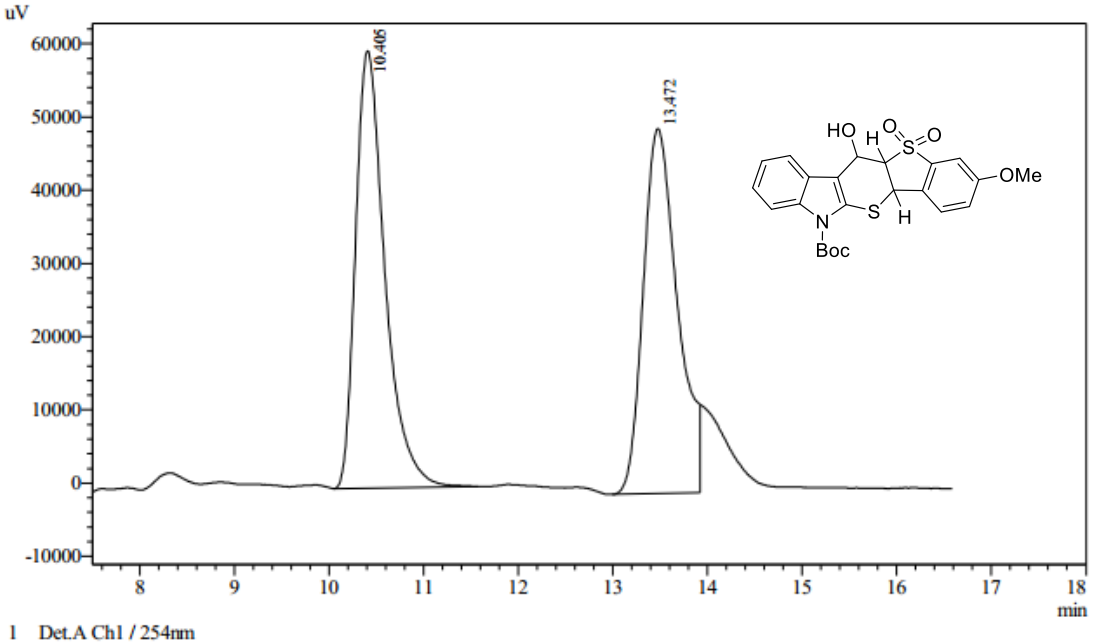
Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.464	2492659	168991	19.301	21.737
2	7.293	10422109	608451	80.699	78.263
Total		12914768	777442	100.000	100.000

^{1}H and ^{13}C NMR of **3t**





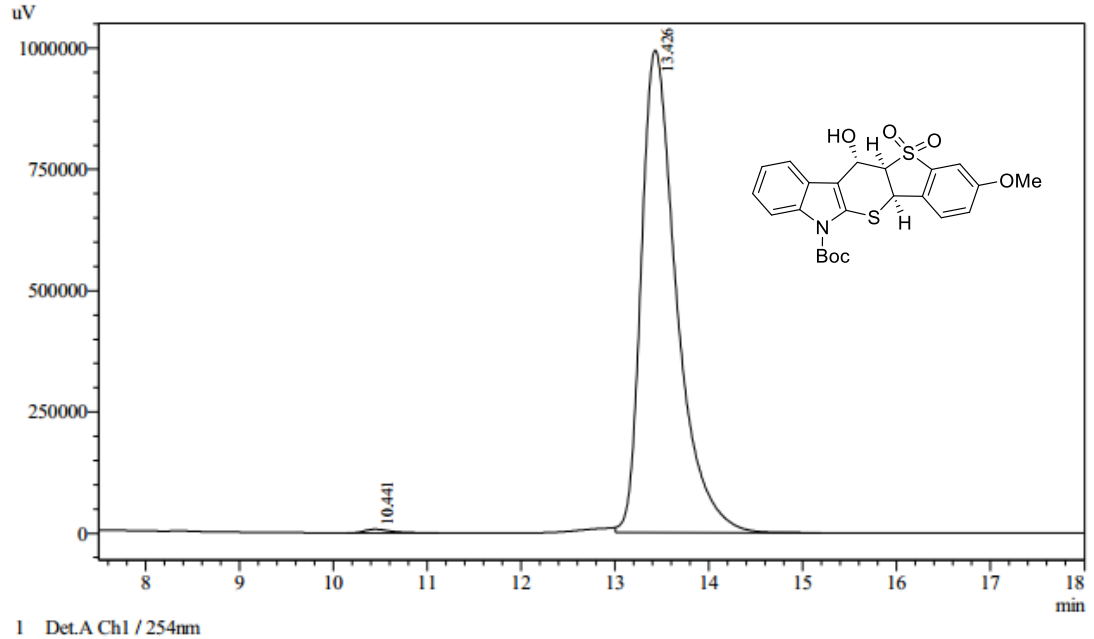
HPLC of **3t**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.405	1289100	59714	50.590	54.505
2	13.472	1259053	49843	49.410	45.495
Total		2548152	109557	100.000	100.000

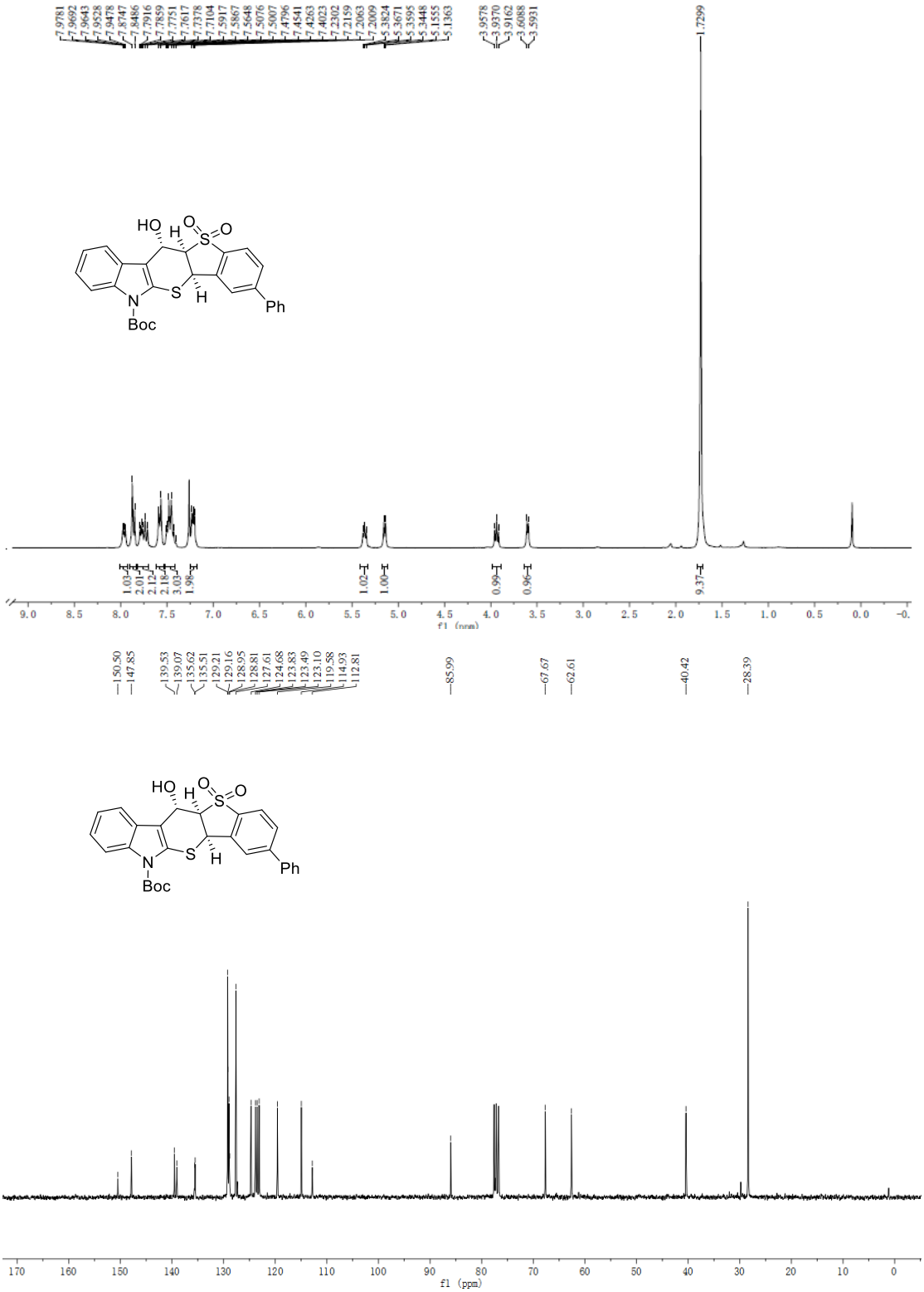


1 Det.A Ch1 / 254nm

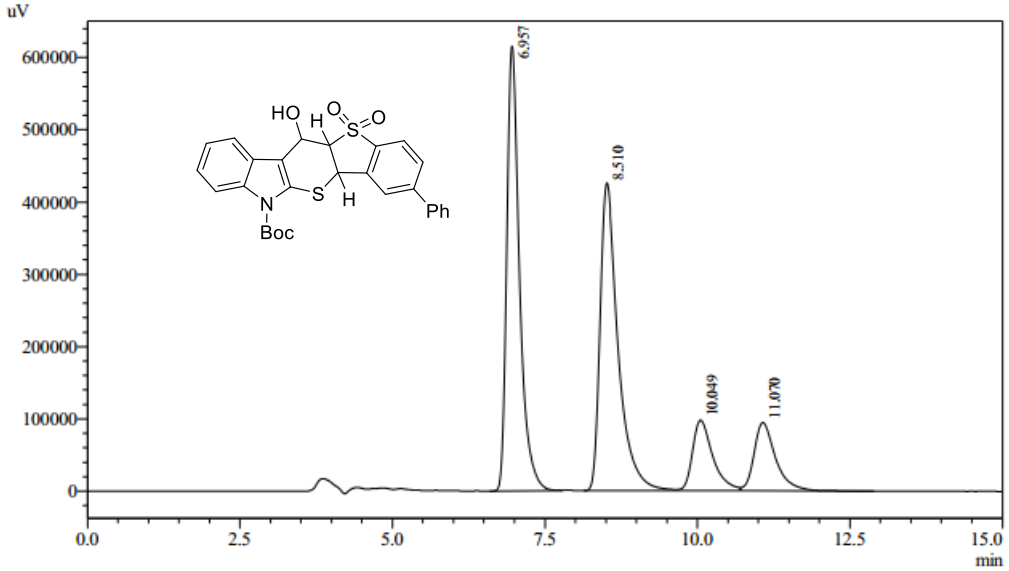
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.441	158660	7892	0.607	0.788
2	13.426	25961766	993987	99.393	99.212
Total		26120426	1001880	100.000	100.000

^{1}H and ^{13}C NMR of **3u**



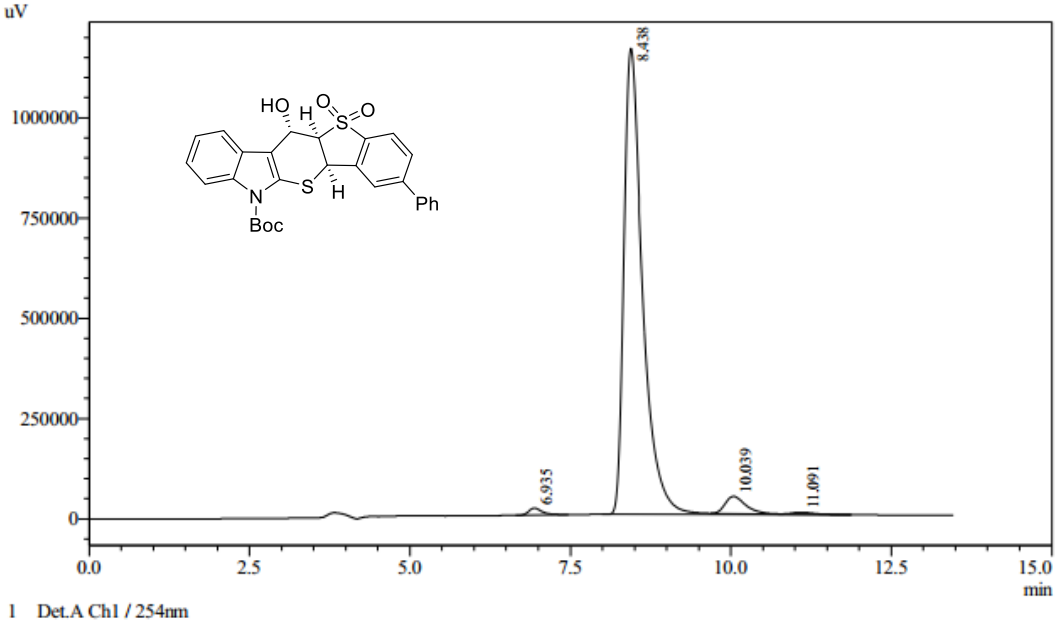
HPLC of **3u**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.957	8846532	615479	39.810	49.902
2	8.510	8808694	425697	39.640	34.515
3	10.049	2248321	97712	10.118	7.922
4	11.070	2318211	94495	10.432	7.661
Total		22221758	1233383	100.000	100.000

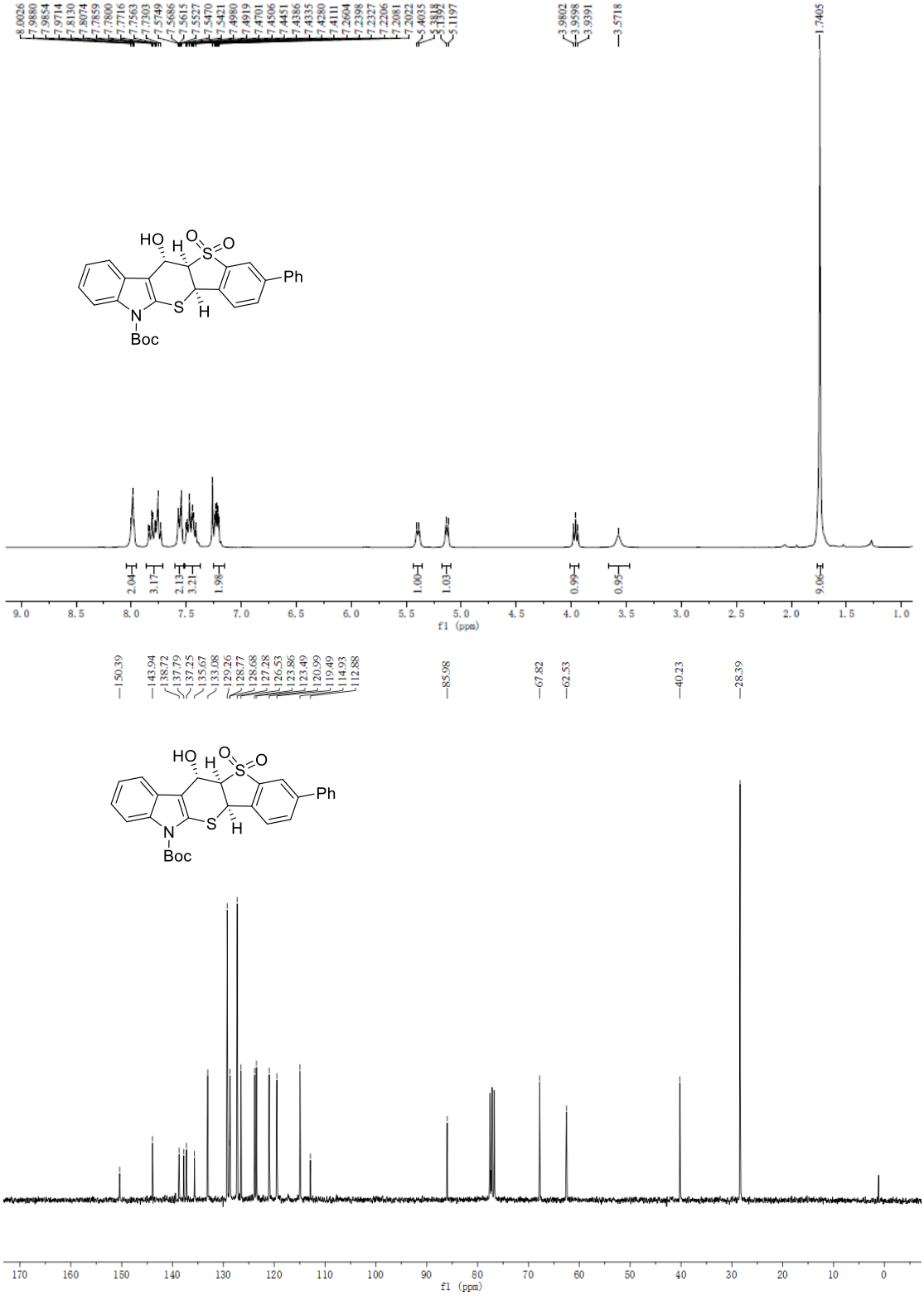


1 Det.A Ch1 / 254nm

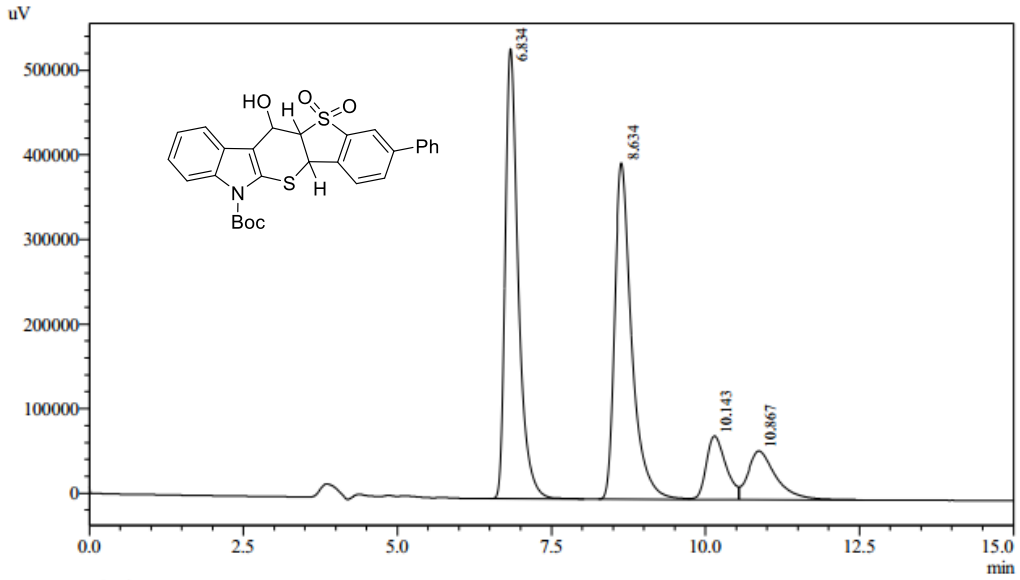
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.935	263569	17763	1.044	1.447
2	8.438	23921493	1161649	94.720	94.644
3	10.039	952020	42952	3.770	3.499
4	11.091	117850	5030	0.467	0.410
Total		25254933	1227393	100.000	100.000

^{1}H and ^{13}C NMR of **3v**



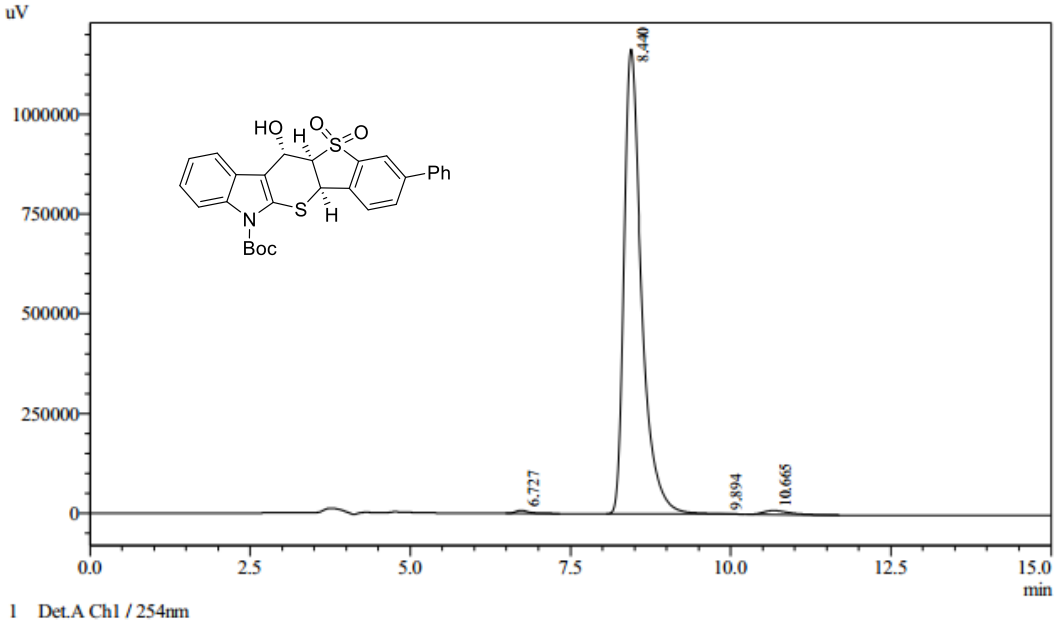
HPLC of **3v**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.834	7780202	531716	40.985	50.064
2	8.634	7721476	397714	40.676	37.447
3	10.143	1659487	75101	8.742	7.071
4	10.867	1821900	57535	9.598	5.417
Total		18983066	1062066	100.000	100.000

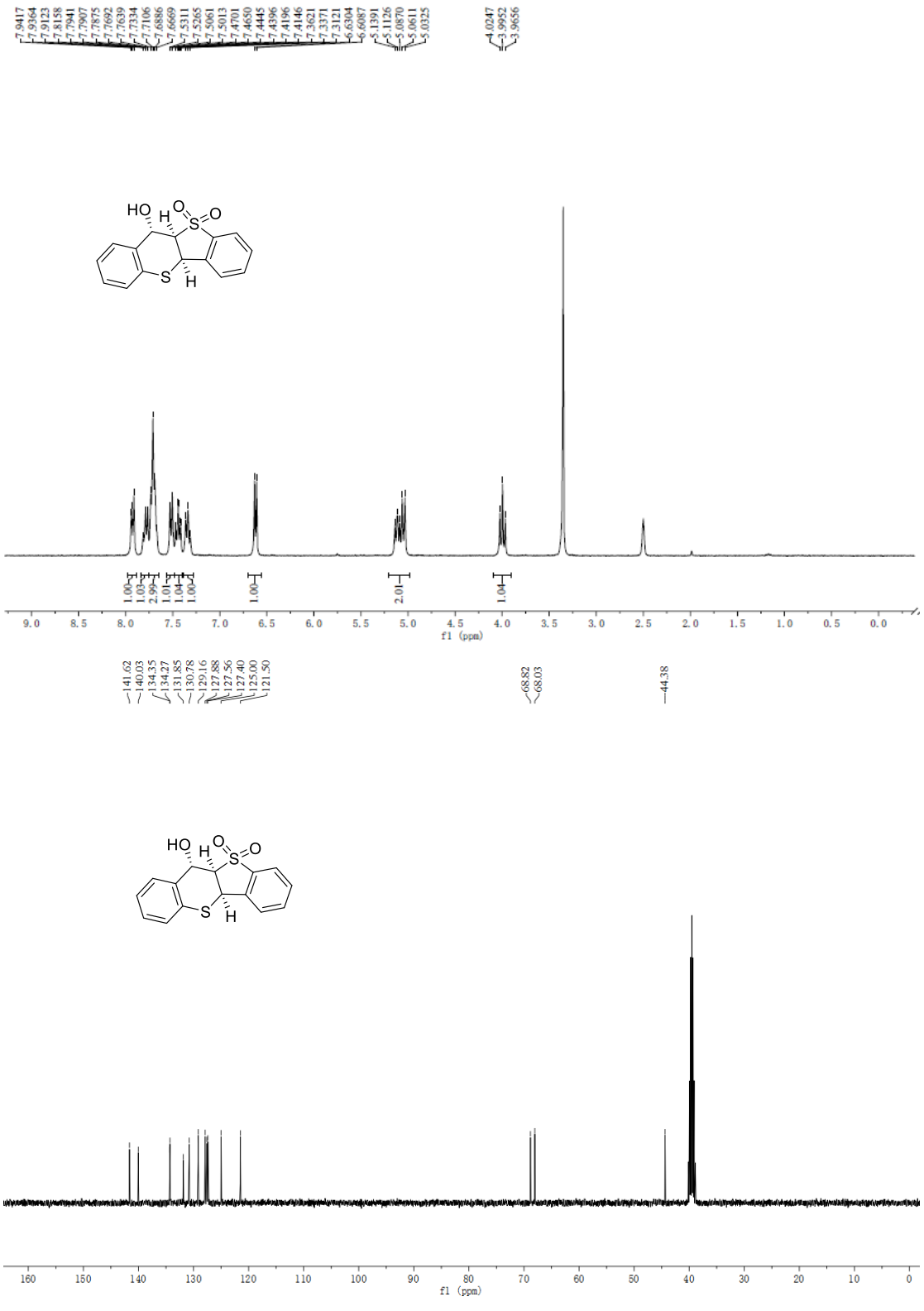


1 Det.A Ch1 / 254nm

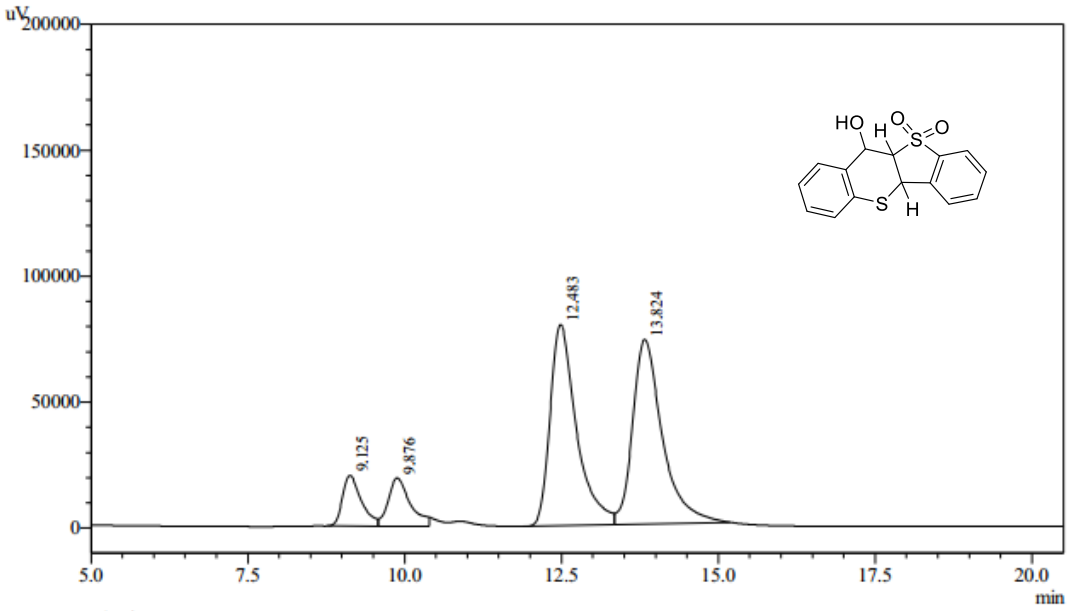
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.727	117828	7805	0.519	0.660
2	8.440	22293564	1164354	98.213	98.475
3	9.894	5726	267	0.025	0.023
4	10.665	282154	9963	1.243	0.843
Total		22699273	1182389	100.000	100.000

^{1}H and ^{13}C NMR of **5a**



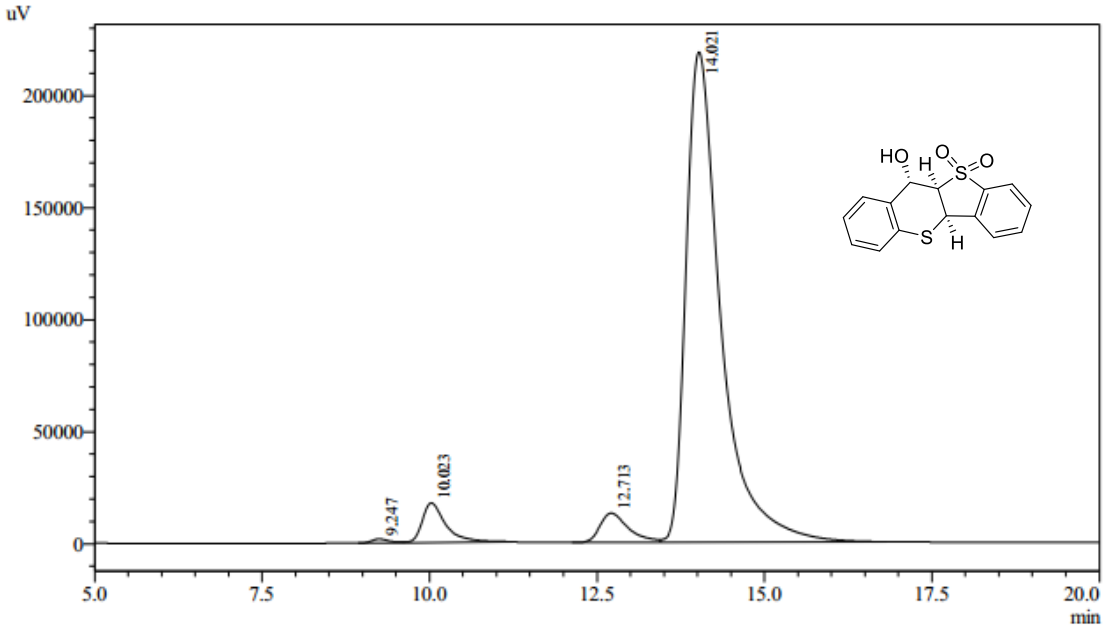
HPLC of **5a**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.125	418112	20084	7.413	10.443
2	9.876	461327	19080	8.179	9.921
3	12.483	2340784	79861	41.500	41.524
4	13.824	2420214	73301	42.908	38.113
Total		5640437	192326	100.000	100.000

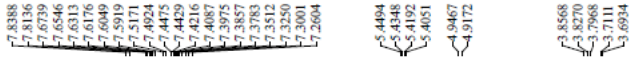


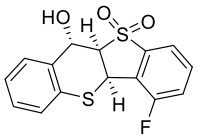
1 Det.A Ch1 / 254nm

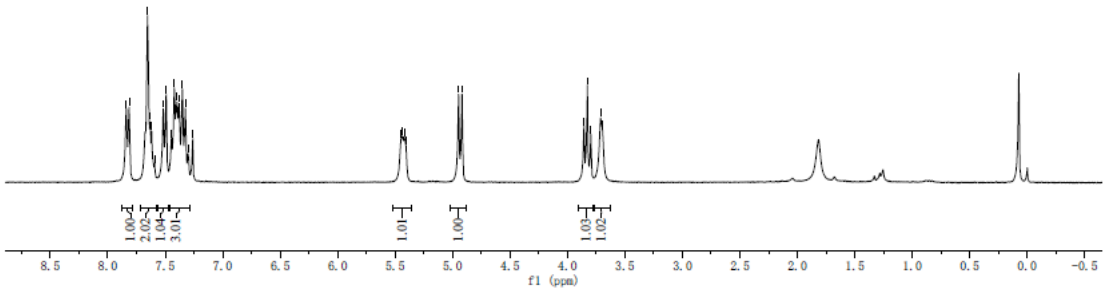
Detector A Ch1 254nm

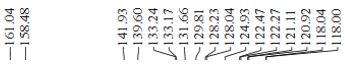
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.247	32437	1765	0.371	0.702
2	10.023	434721	17680	4.970	7.034
3	12.713	389272	13076	4.450	5.203
4	14.021	7890704	218822	90.209	87.061
Total		8747134	251343	100.000	100.000

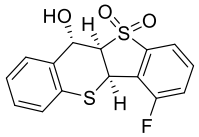
^{1}H and ^{13}C NMR of **5b**



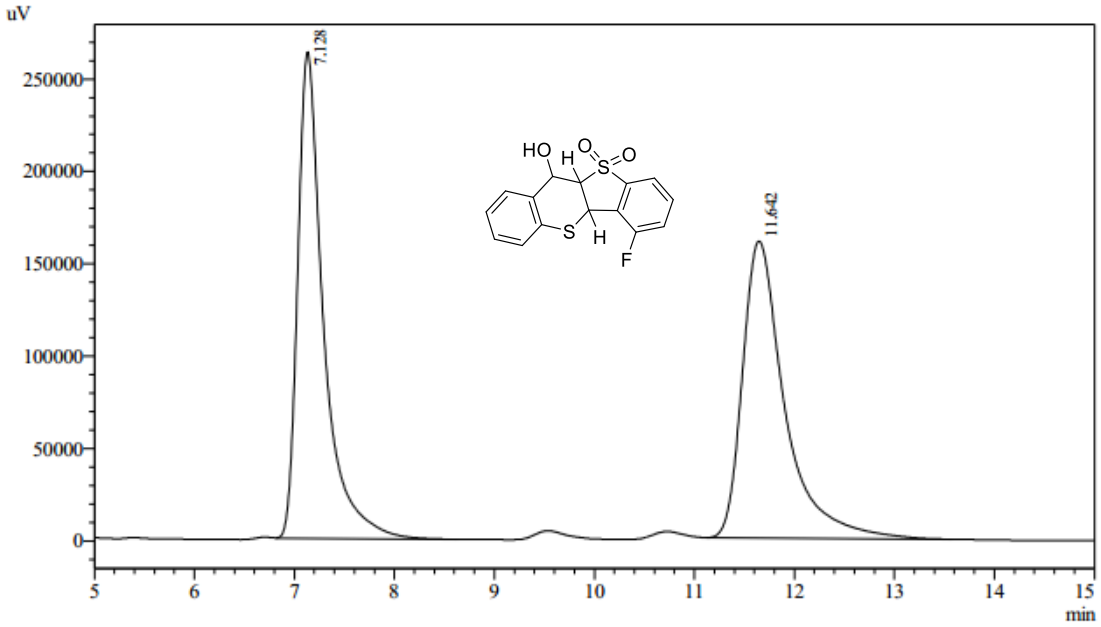






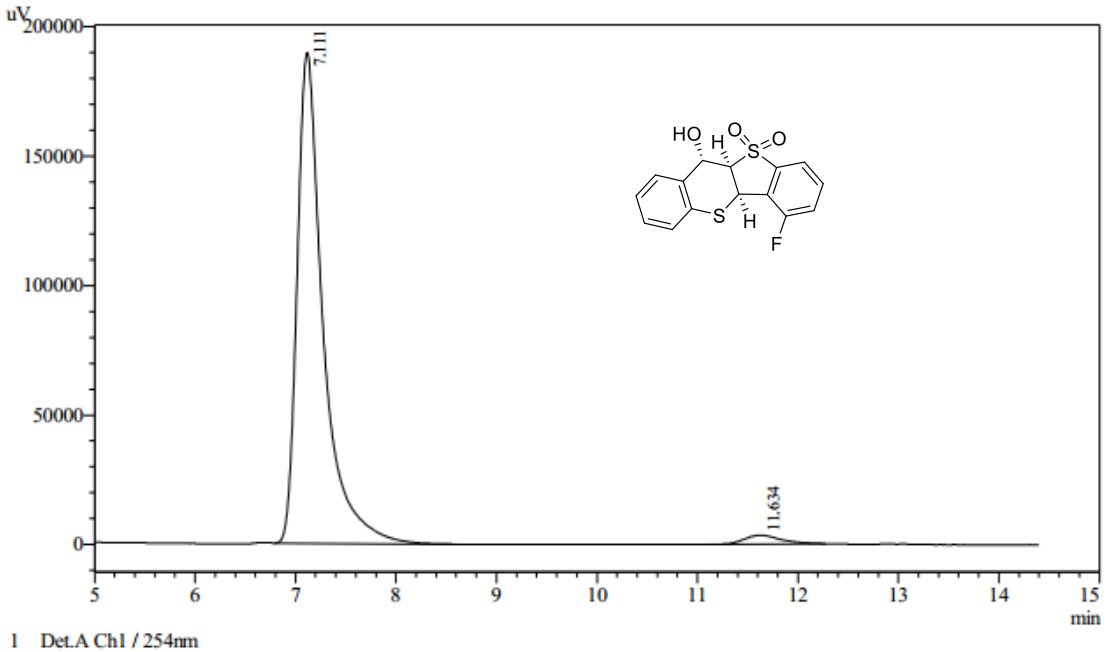


HPLC of **5b**



Detector A Ch1 254nm

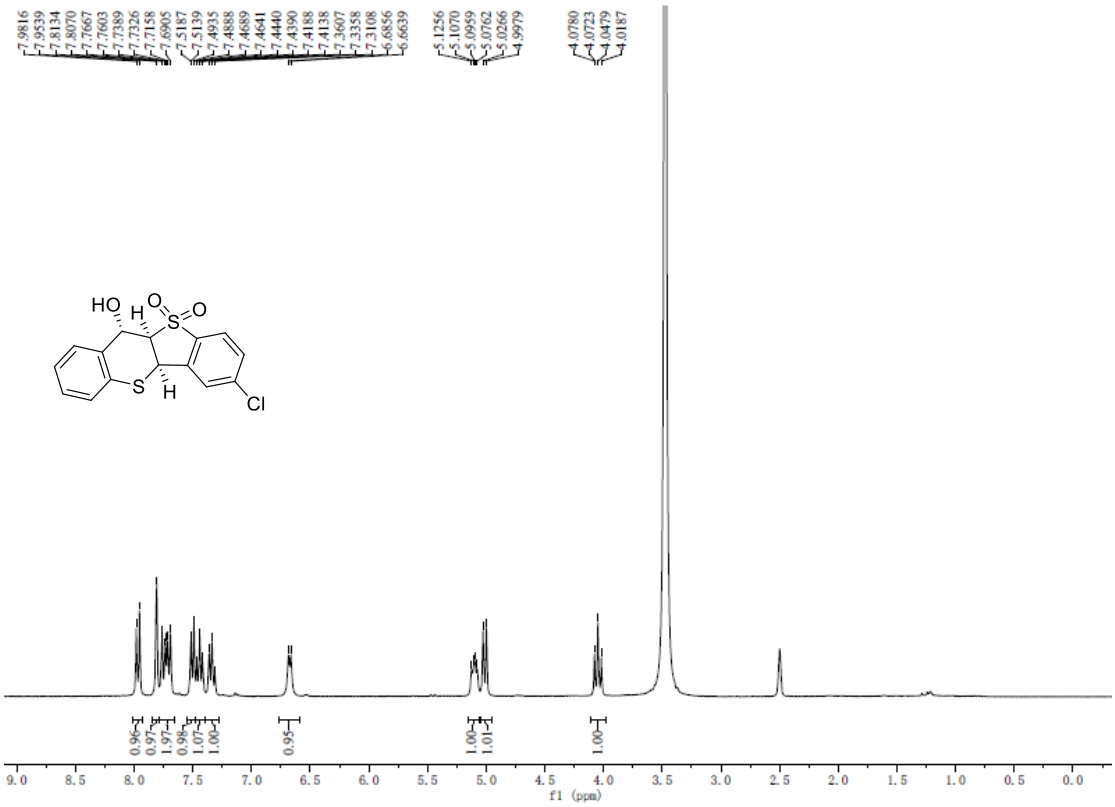
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.128	4744605	263345	50.079	62.089
2	11.642	4729560	160794	49.921	37.911
Total		9474165	424139	100.000	100.000

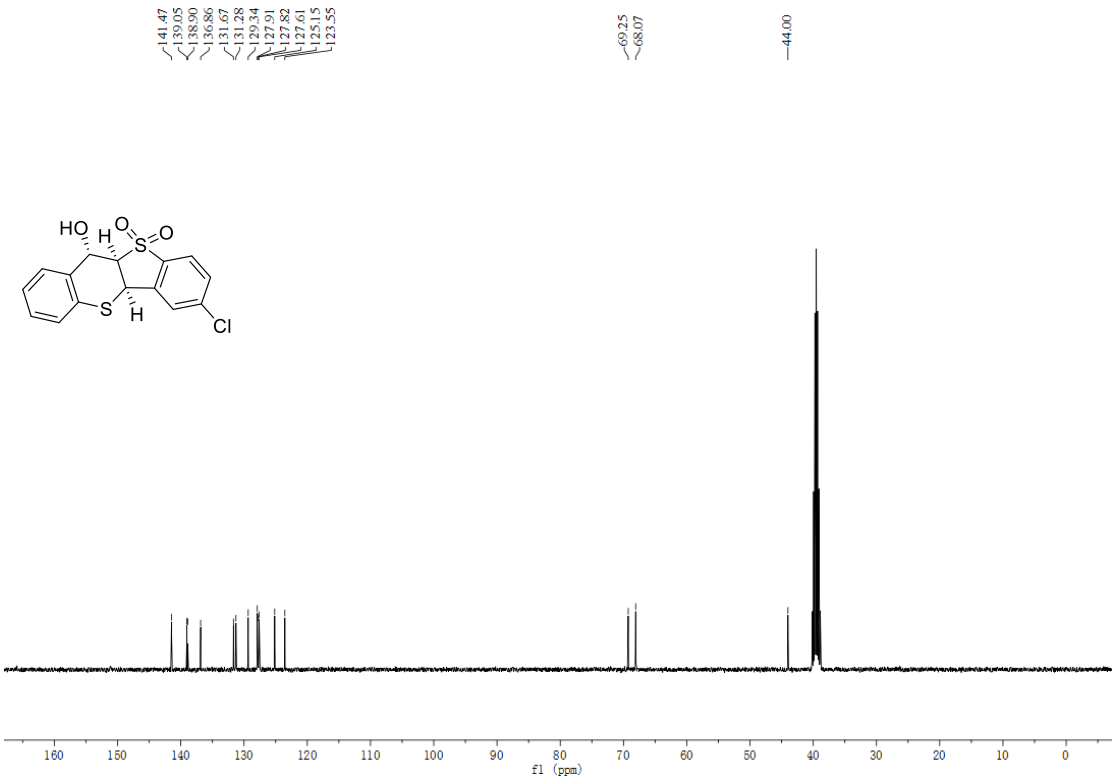


Detector A Ch1 254nm

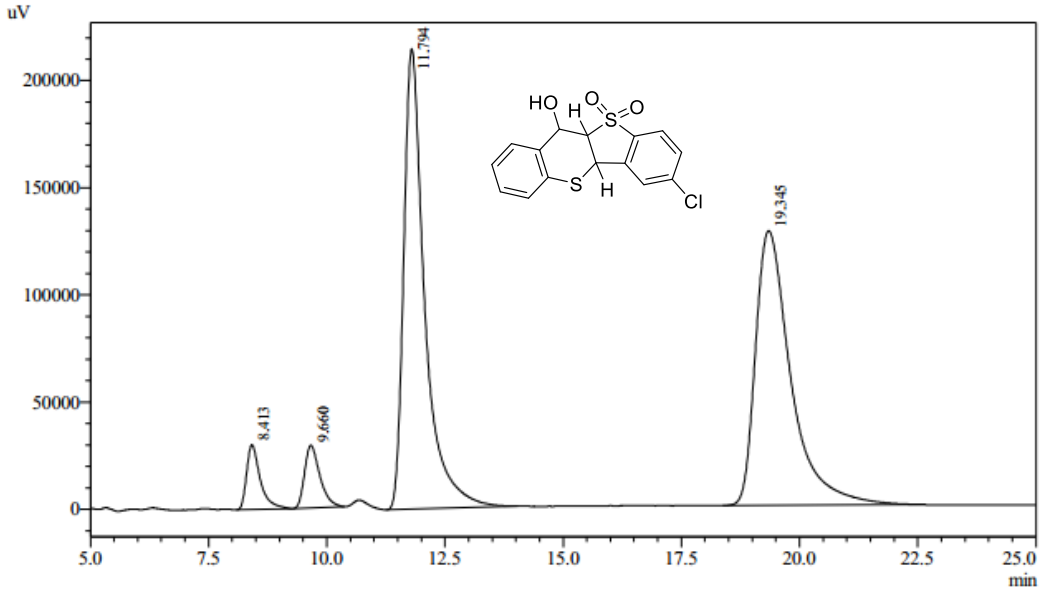
Peak#	Ret. Time	Area	Height	Area %	Height %
1	7.111	3412322	189371	97.457	98.223
2	11.634	89033	3426	2.543	1.777
Total		3501355	192797	100.000	100.000

^{1}H and ^{13}C NMR of **5c**





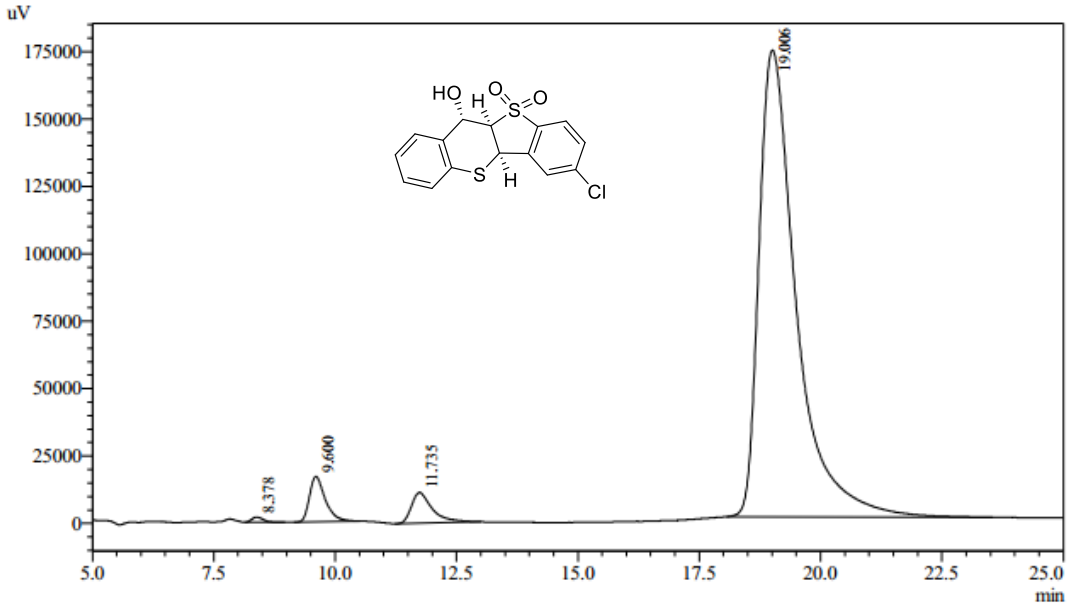
HPLC of **5c**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.413	608286	30221	4.170	7.511
2	9.660	662341	29256	4.540	7.271
3	11.794	6639431	214829	45.511	53.391
4	19.345	6678661	128064	45.780	31.827
Total		14588719	402369	100.000	100.000

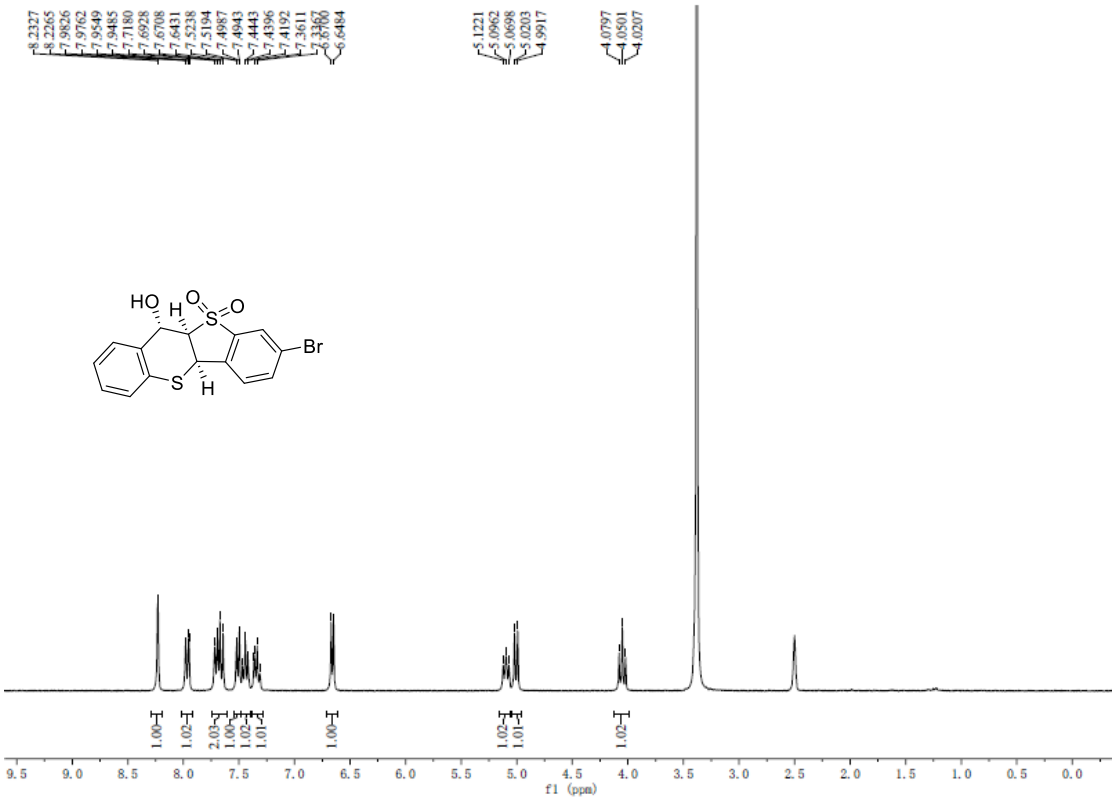


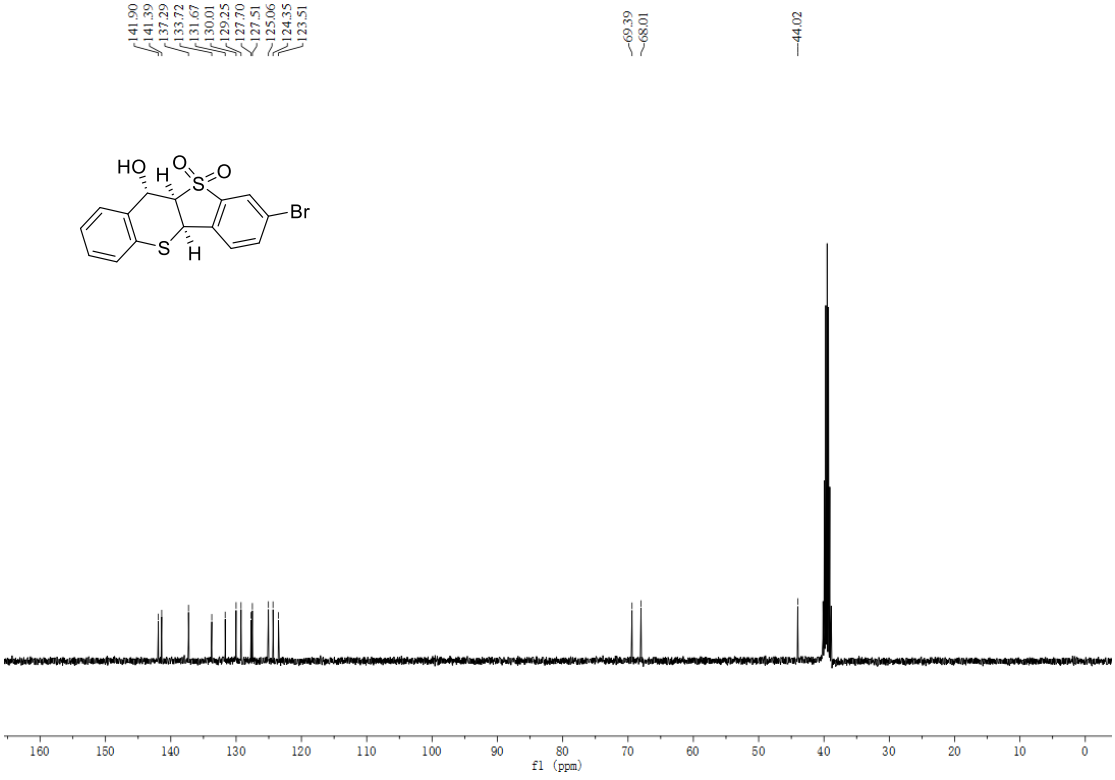
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

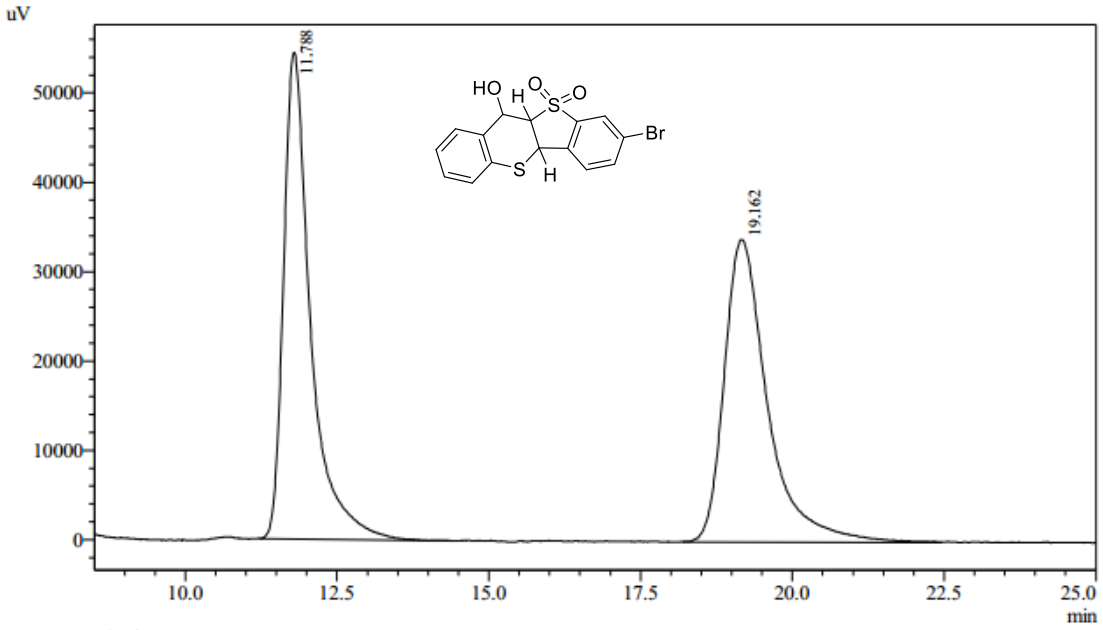
Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.378	29619	1859	0.297	0.915
2	9.600	379501	16863	3.800	8.301
3	11.735	343292	11378	3.437	5.601
4	19.006	9234517	173035	92.466	85.182
Total		9986929	203134	100.000	100.000

^{1}H and ^{13}C NMR of **5d**





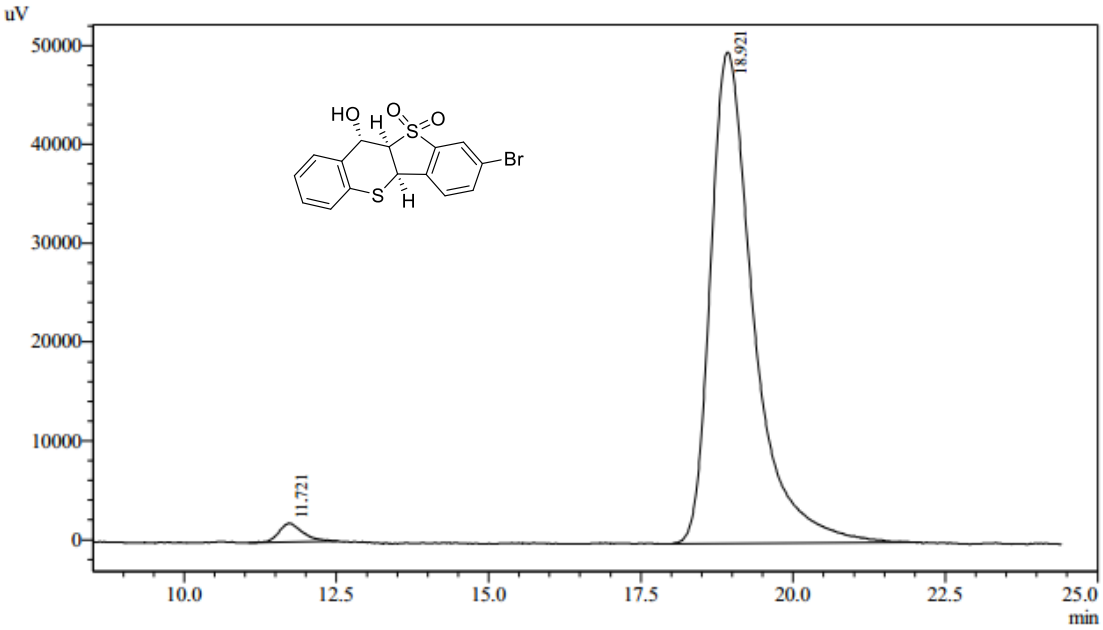
HPLC of **5d**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.788	1685254	54473	50.016	61.666
2	19.162	1684187	33863	49.984	38.334
Total		3369442	88336	100.000	100.000

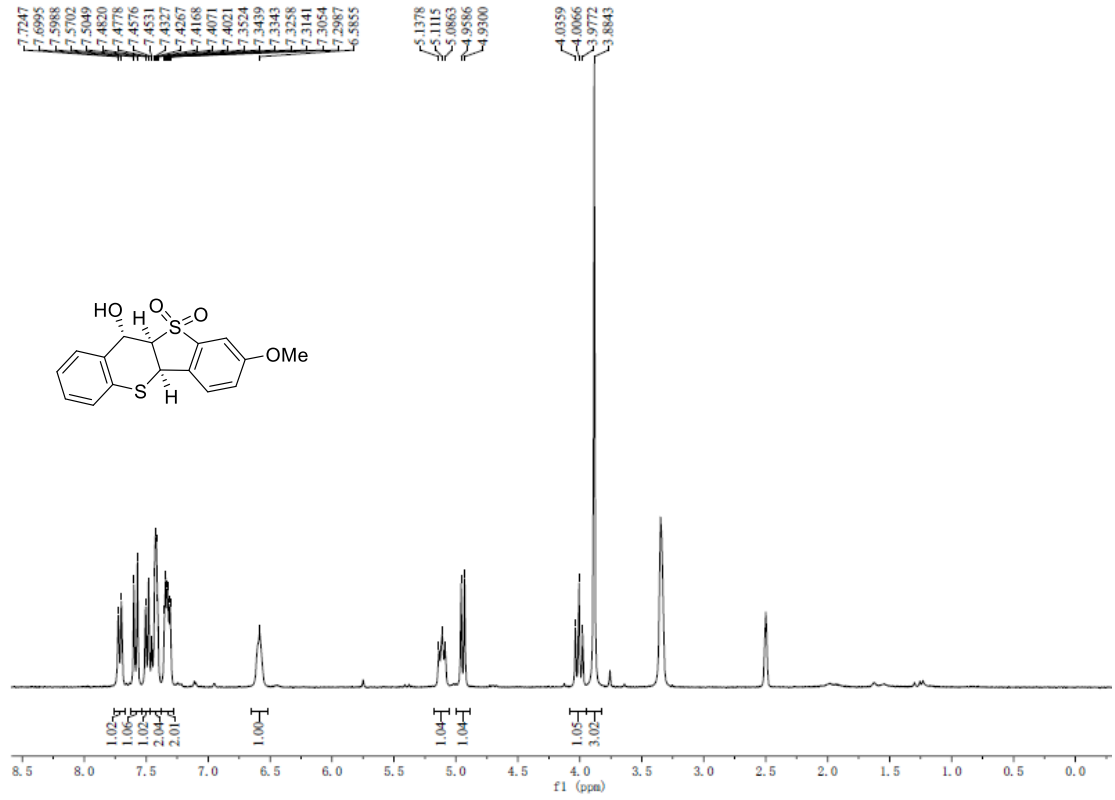


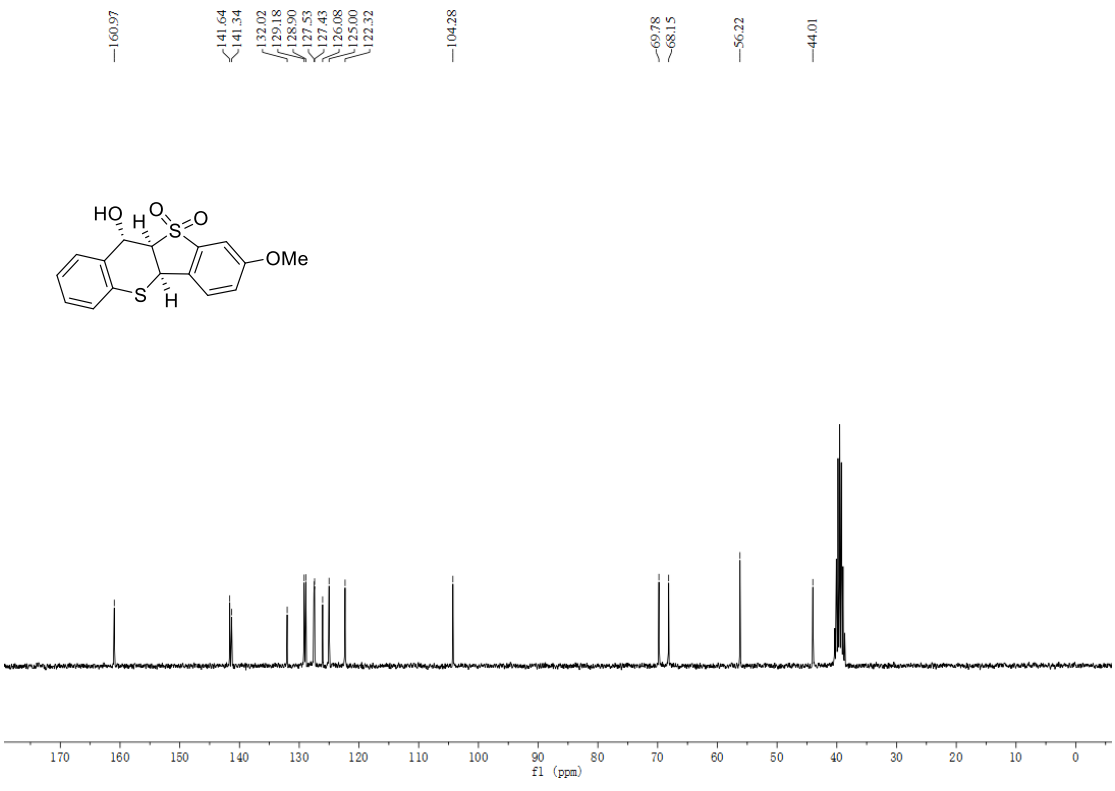
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

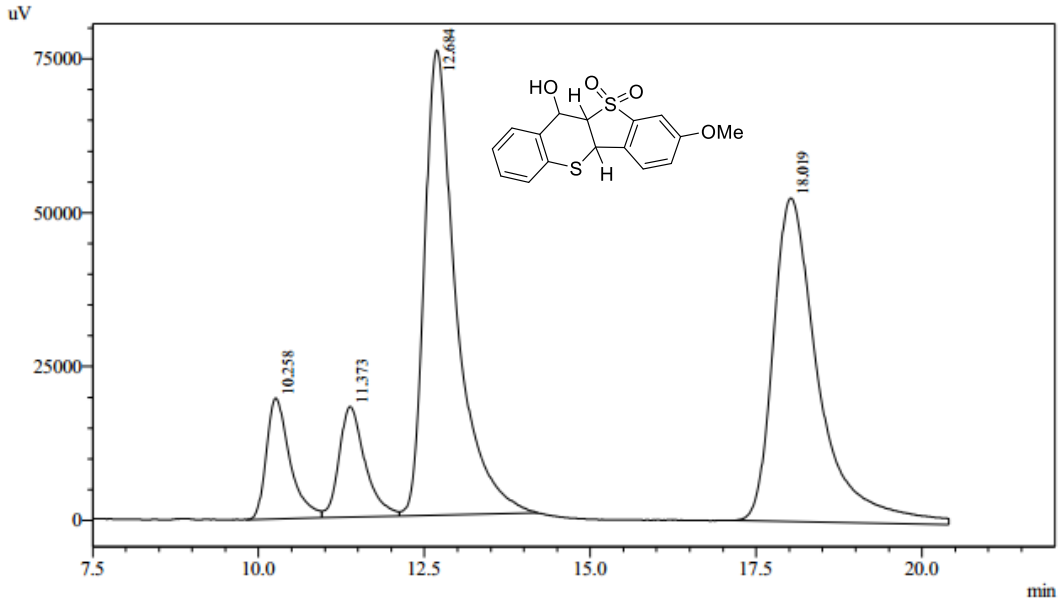
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.721	52481	1909	2.100	3.701
2	18.921	2446729	49680	97.900	96.299
Total		2499210	51590	100.000	100.000

^{1}H and ^{13}C NMR of **5e**





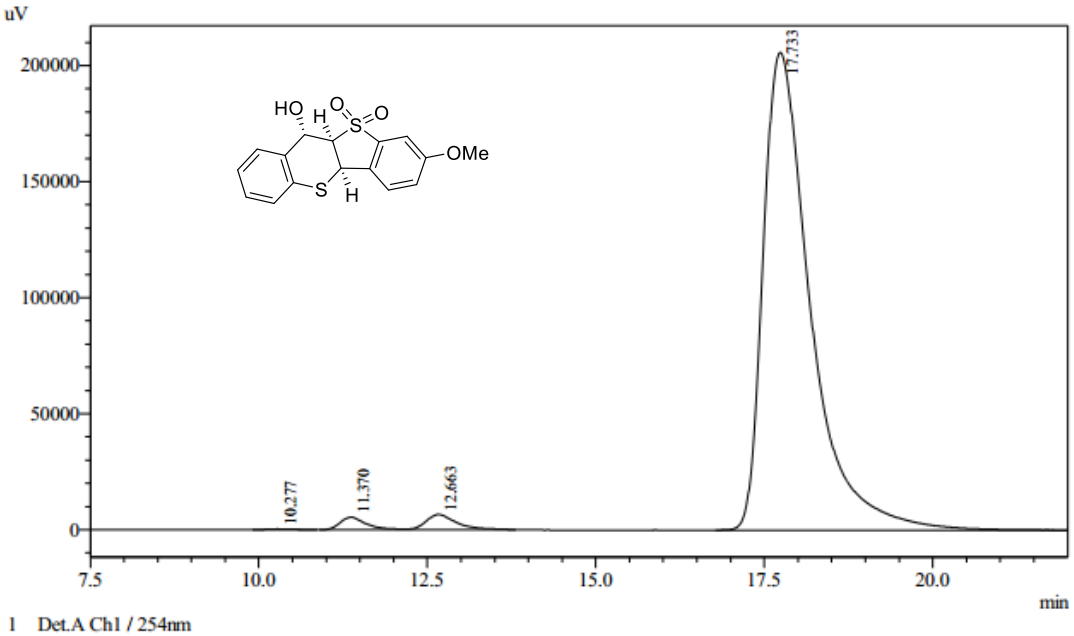
HPLC of **5e**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.258	487278	19627	8.100	11.840
2	11.373	493168	17995	8.198	10.856
3	12.684	2534124	75569	42.127	45.589
4	18.019	2500871	52572	41.574	31.715
Total		6015441	165763	100.000	100.000

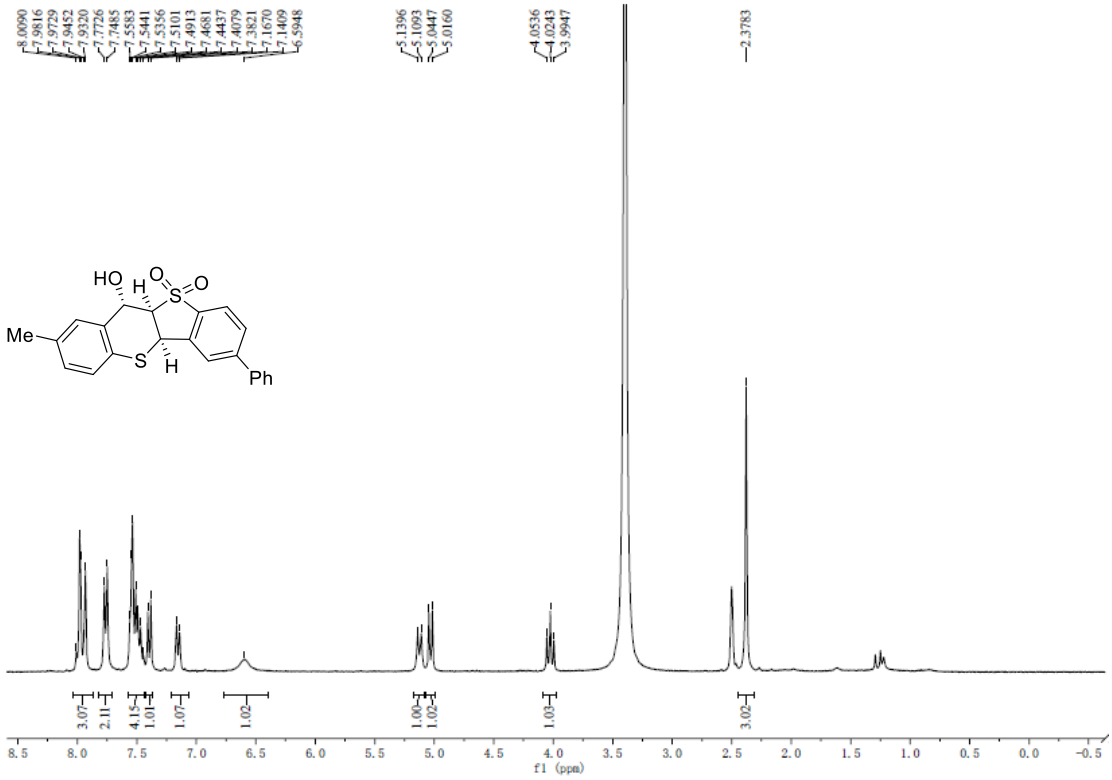


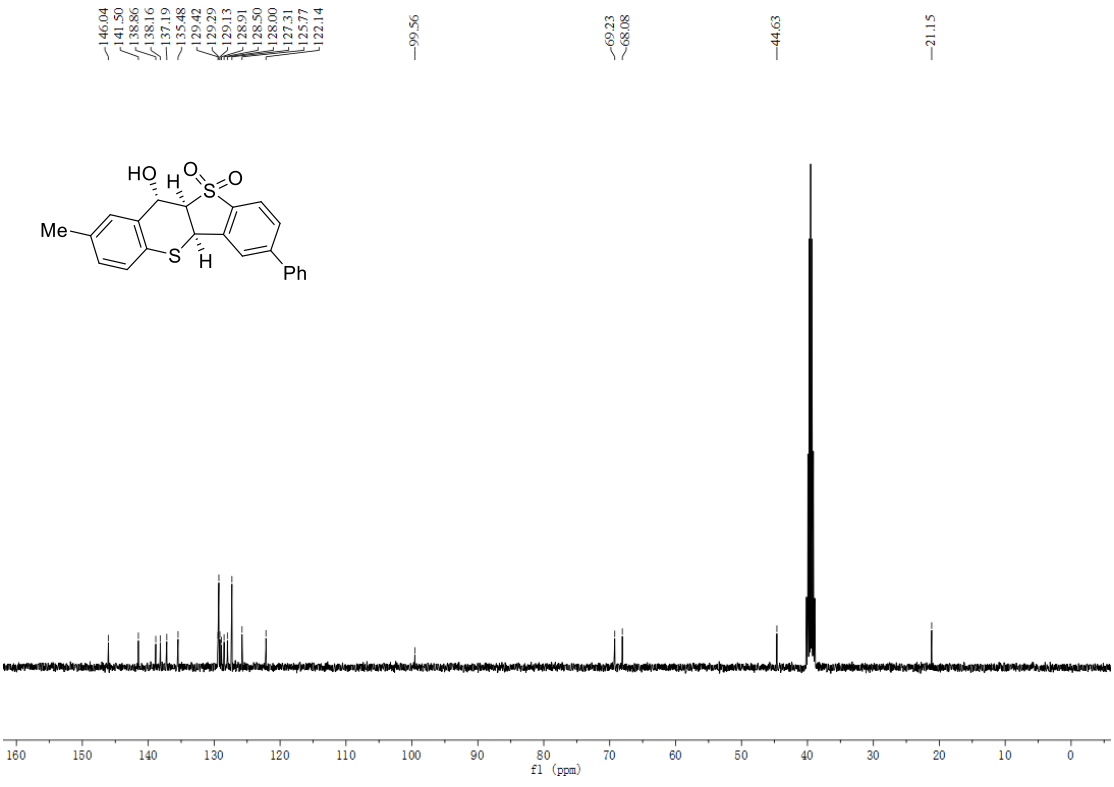
1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

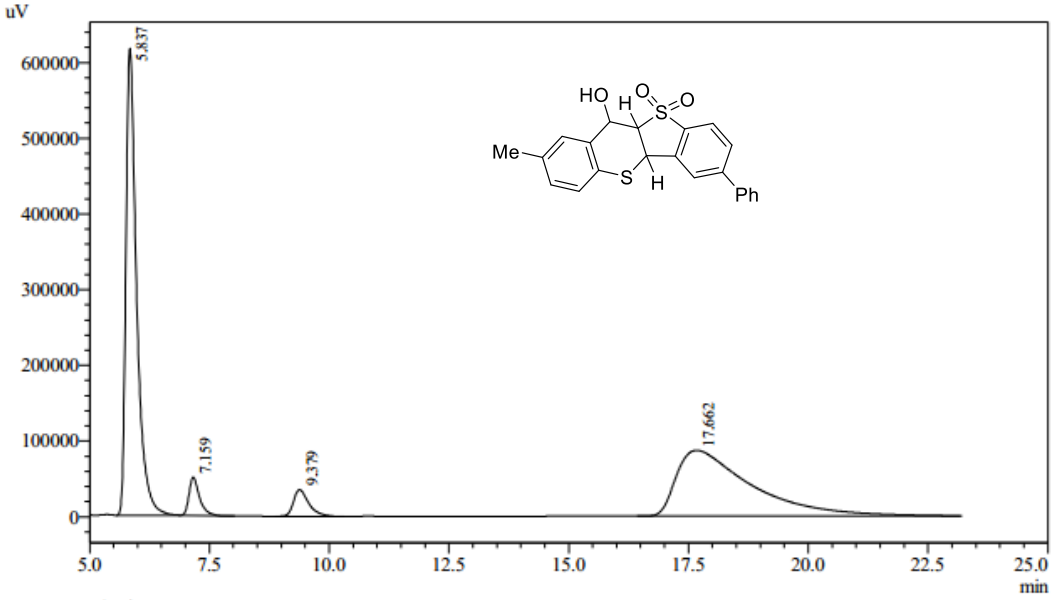
Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.277	7901	350	0.076	0.161
2	11.370	142508	5325	1.370	2.442
3	12.663	201199	6497	1.934	2.979
4	17.733	10053881	205877	96.621	94.418
Total		10405489	218049	100.000	100.000

^{1}H and ^{13}C NMR of **5f**





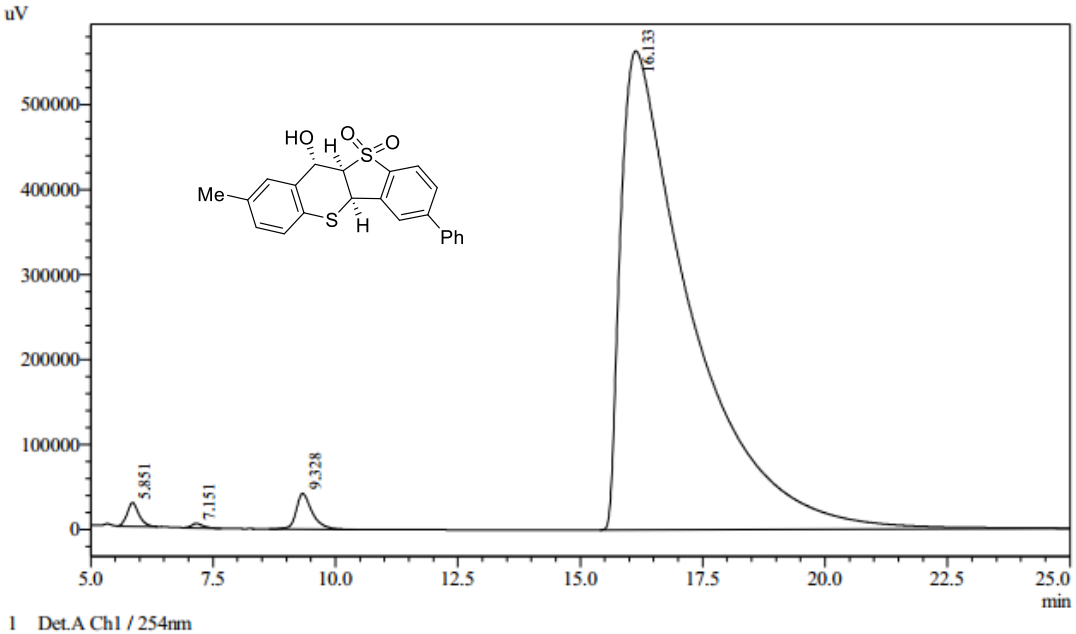
HPLC of **5f**



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.837	9548782	616826	46.621	78.133
2	7.159	769251	50547	3.756	6.403
3	9.379	780494	35230	3.811	4.463
4	17.662	9383134	86851	45.812	11.001
Total		20481660	789455	100.000	100.000



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.851	460010	28004	0.793	4.383
2	7.151	82945	5282	0.143	0.827
3	9.328	951852	41959	1.642	6.568
4	16.133	56479686	563629	97.422	88.222
Total		57974493	638874	100.000	100.000